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The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6) 5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes Xhol/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heatinactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS

(Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as  $5 \times 10^5$  cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1x10<sup>5</sup> cells/well). Add 50 ul supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

## Example 16: High-Throughput Screening Assay for T-cell Activity

NF-kB (Nuclear Factor kB) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-kB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- kB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- κB is retained in the cytoplasm with I-κB (Inhibitor κB). However, upon stimulation, I- κB is phosphorylated and degraded, causing NF- κB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- κB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-kB promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF-kB would be useful in treating diseases. For example, inhibitors of NF-kB could be used to treat those

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diseases related to the acute or chronic activation of NF-kB, such as rheumatoid arthritis.

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The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

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## 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

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PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene)
Sequencing with the T7 and T3 primers confirms the insert contains the following

sequence:

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5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGACTTTCC
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCGCCCCTAACTCCGCCC
ATCCCGCCCCTAACTCCGCCCAGTTCCGCCCCATGGCTGA
CTAATTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTA
TTCCAGAAGTAGTGAGGAGGCTTTTTTTGGAGGCCTAGGCTTTTTGCAAAAA
GCTT:3' (SEO ID NO:10)

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Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-xB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

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In order to generate stable mammalian cell lines, the NF-kB/SV40/SEAP cassette is removed from the above NF-kB/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly,

the NF-kB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and Notl.

Once NF-kB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 13. As a positive control, exogenous TNF alpha (0.1,1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

### Example 17: Assay for SEAP Activity

As a reporter molecule for the assays described in Examples 13-16, SEAP. activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15  $\mu$ l of 2.5x dilution buffer into Optiplates containing 35  $\mu$ l of a supernatant. Seal the plates with a plastic scaler and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 µl Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 µl Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

#### Reaction Buffer Formulation:

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5

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5			336	
	13	75 '	3.75	
	14	80	4	•
	15	85	4.25	
10	16	90	4.5	
	17	95	4.75	
	18	100	5	
	19	105	5.25	
15	20	110	5.5	
	21	115	5.75	
	. 22	120	6	
	23	125	6.25	
20	24	130	6.5	
	25	135	6.75	•
	26	140	7	
	27	145	7.25	
	28	150	7.5	
25	29	155	7.75	
	30	160	8	
	31	165	8.25	•
	32	170	8.5	
30	33	175	8.75	
	34	180	9	
	35	185	9.25	•
	36	190	9.5	
35	37	195	9.75	
	38	200	10	
	39	205	10.25	•
	40	210	10.5	
40	41	215	10.75	
40	42	220	11	
	43	225	11.25	
	44	230	11.5	
	. 45	235	11.75	
45	46	240	12	
	47	245	12.25	
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# Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

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Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-4 (Molecular Probes, Inc.; catalog no. F-14202), used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO<sub>2</sub> incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-4 is made in 10% pluronic acid DMSO. To load the cells with fluo-4, 50 ul of 12 ug/ml fluo-4 is added to each well. The plate is incubated at 37°C in a CO<sub>2</sub> incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10<sup>6</sup> cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-4 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10<sup>6</sup> cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200 ul, followed by an aspiration step to 100 ul final volume.

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For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-4. The supernatant is added to the well, and a change in fluorescence is detected.

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To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca++ concentration.

Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase **Activity** 

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of activating the tyrosine kinase signal transduction pathways.

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Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford,MA), or calf serum, rinsed with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford,MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na3VO4, 2 mM Na4P2O7 and a cocktail of protease inhibitors (# 1836170) obtained from Boeheringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg<sub>2+</sub> (5mM ATP/50mM MgCl<sub>2</sub>), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM bcta-glycerophosphate, 1mM EGTA, 100mM MgCl<sub>2</sub>, 5 mM MnCl<sub>2</sub>, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30°C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mm EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavadin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phospotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

# Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity

As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (lug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this

and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place

of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (lug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive

incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

Example 21: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Manheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for

precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

# Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

## Example 23: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about I µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to

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modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semipermeable polymer matrices in the form of shaped articles, e.g., films, or mirocapsules. Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22:547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer, et al., J. Biomed. Mater. Res. 15:167-277 (1981), and R. Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D-(-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. USA 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilarmellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's

solution, and dextrosc solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulos.

polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in

the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

# Example 24: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 23.

## 20 Example 25: Method of Treating Increased Levels of the Polypeptide

Antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 23.

Example 26: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

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Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

# Example 27: Method of Treatment Using Gene Therapy - In Vivo

Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide. The polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art, see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata H. et al. (1997) Cardiovasc. Res. 35(3):470-479, Chao J et al. (1997) Pharmacol. Res. 35(6):517-522, Wolff J.A. (1997) Neuromuscul. Disord. 7(5):314-318, Schwartz B. et al. (1996) Gene Ther. 3(5):405-411, Tsurumi Y. et al. (1996) Circulation 94(12):3281-3290 (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The

polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

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The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) Ann. NY Acad. Sci. 772:126-139 and Abdallah B. et al. (1995) Biol. Cell 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely

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differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. In vivo muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle in vivo is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A

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time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

#### Example 28: Transgenic Animals.

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e.g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans. as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (i.e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40:691-698 (1994); Carver et al., Biotechnology (NY) 11:1263-1270 (1993); Wright et al., Biotechnology (NY) 9:830-834 (1991); and Hoppe et al., U.S. Pat. No. 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82:6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56:313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3:1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e.g., Ulmer et al., Science 259:1745 (1993); introducing nucleic acid constructs into embryonic pleuripotent stem cells and transferring the stem cells back into the blastocyst; and spermmediated gene transfer (Lavitrano et al., Cell 57:717-723 (1989); etc. For a review of such techniques, see Gordon, "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989), which is incorporated by reference herein in its entirety.

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Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380:64-66 (1996); Wilmut et al., Nature 385:810-813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, i.e., mosaic animals or chimeric. The transgene may be integrated as a single transgene or as multiple, copies such as in concatamers, e.g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci. USA 89:6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265:103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse

transcriptase-PCR (rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate tines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in claborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

#### Example 29: Knock-Out Animals.

Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (E.g., see Smithies et al., Nature 317:230-234 (1985); Thomas & Capecchi, Cell 51:503-512 (1987); Thompson et al., Cell 5:313-321 (1989); each of which is incorporated by reference herein in its entirety). For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention in vivo. In another embodiment, techniques known in

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the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such approaches are particularly suited in research and agricultural fields where modifications to embryonic stem cells can be used to generate animal offspring with an inactive targeted gene (e.g., see Thomas & Capecchi 1987 and Thompson 1989, supra). However this approach can be routinely adapted for use in humans provided the recombinant DNA constructs are directly administered or targeted to the required site in vivo using appropriate viral vectors that will be apparent to those of skill in the art.

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In further embodiments of the invention, cells that are genetically engineered to express the polypeptides of the invention, or alternatively, that are genetically engineered not to express the polypeptides of the invention (e.g., knockouts) are administered to a patient in vivo. Such cells may be obtained from the patient (i.e., animal, including human) or an MHC compatible donor and can include, but are not limited to fibroblasts, bone marrow cells, blood cells (e.g., lymphocytes), adipocytes, muscle cells, endothelial cells etc. The cells are genetically engineered in vitro using recombinant DNA techniques to introduce the coding sequence of polypeptides of the invention into the cells, or alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence associated with the polypeptides of the invention, e.g., by transduction (using viral vectors, and preferably vectors that integrate the transgene into the cell genome) or transfection procedures, including, but not limited to, the use of plasmids, cosmids, YACs, naked DNA, electroporation, liposomes, etc. The coding sequence of the polypeptides of the invention can be placed under the control of a strong constitutive or inducible promoter or promoter/enhancer to achieve expression, and preferably secretion, of the polypeptides of the invention. The engineered cells which express and preferably secrete the polypeptides of the invention can be introduced into the patient systemically, e.g., in the circulation, or intraperitoneally.

Alternatively, the cells can be incorporated into a matrix and implanted in the body, <u>e.g.</u>, genetically engineered fibroblasts can be implanted as part of a skin graft; genetically engineered endothelial cells can be implanted as part of a lymphatic or vascular graft. (See, for example, Anderson et al. U.S. Patent No. 5,399,349; and

Mulligan & Wilson, U.S. Patent No. 5,460,959 each of which is incorporated by reference herein in its entirety).

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When the cells to be administered are non-autologous or non-MHC compatible cells, they can be administered using well known techniques which prevent the development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

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Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

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It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

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The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties.

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## Claims

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#### What Is Claimed Is:

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l.	An isolated nucleic acid molecule comprising a polynucleotide having
a nucleotide s	equence at least 95% identical to a sequence selected from the group
consisting of:	•

- (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
- (e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;
  - (f) a polynucleotide which is a variant of SEQ ID NO:X;
  - (g) a polynucleotide which is an allelic variant of SEQ ID NO:X;
- (h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
- (i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
- 2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.

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3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

- 4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.
- 5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
- The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
- 7. A recombinant vector comprising the isolated nucleic acid molecule of claim I.
- 8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
  - A recombinant host cell produced by the method of claim 8.
  - 10. The recombinant host cell of claim 9 comprising vector sequences.
- 11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

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	(a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence			
	included in ATCC Deposit No:Z;			
10	(b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence			
	included in ATCC Deposit No:Z, having biological activity;			
	(c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included			
	in ATCC Deposit No:Z;			
15	(d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included			
	in ATCC Deposit No:Z;			
	(e) a secreted form of SEQ ID NO:Y or the encoded sequence included in			
20	ATCC Deposit No:Z;			
20	(f) a full length protein of SEQ ID NO:Y or the encoded sequence included in			
	ATCC Deposit No:Z;			
	(g) a variant of SEQ ID NO:Y;			
25	(h) an allelic variant of SEQ ID NO:Y; or			
	(i) a species homologue of the SEQ ID NO:Y.			
	12. The isolated polypeptide of claim 11, wherein the secreted form or the			
	full length protein comprises sequential amino acid deletions from either the C-			
30	terminus or the N-terminus.			
	13. An isolated antibody that binds specifically to the isolated polypeptide			
35	of claim 11.			
	14. A recombinant host cell that expresses the isolated polypeptide of			
	claim 11.			
40				
	15. A method of making an isolated polypeptide comprising:			
	(a) culturing the recombinant host cell of claim 14 under conditions such that			
	said polypeptide is expressed; and			
45	(b) recovering said polypeptide.			
	<ol><li>The polypeptide produced by claim 15.</li></ol>			
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17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polypucleotide of claim 1.

- 18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.
- 19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:
- (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.
- 20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
  - (a) contacting the polypeptide of claim 11 with a binding partner; and
- (b) determining whether the binding partner effects an activity of the polypeptide.
  - 21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
- 22. A method of identifying an activity in a biological assay, wherein the method comprises:
  - (a) expressing SEQ ID NO:X in a cell;
  - (b) isolating the supernatant;
  - (c) detecting an activity in a biological assay; and
  - (d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

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<sup>&</sup>lt;210> 30

<sup>&</sup>lt;211> 2227

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Homo sapiens

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720

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catcagggtt cartgcacag gageeteata cacactacag aaaatatget ettgtaacee
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2280
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gccctgcagg ccctgcaagg agagetetet gaggttatte teagetteag eteceteaat

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1680

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420

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<221> STTE
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cotgetttee tgeccectee etectetgtg cotgectgee tetgetgtge egggecagtg
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                                                                     1260
 1320
 азававава вазававава завававава вдудсудсту с
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                                                                    420
atcaacaatg ctggggtgat gatggtccct cagaggaaaa ccagagatgg attcgaagaa
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1020

1080

1140

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catchatacc ammangetett acceptetett tagaaggama atatttgtat cetetattcc
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                                                                         960
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ttactgatct acaaccggtt ttaagttagt tgcctgctta aaattttctc atgaattctc
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toatttacta etgitacett cettatteat tecatteeae ecacagtgge ettettgeaa
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gtcagagaat gcaacaaata tgctcctgcc ttggggcatt tgcacttctg ttcttttggc
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ctggtcactt cacctccaca ttctccattt trtatgactt tcttcctata tttggatctc
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tgttcasatg tcacccctca aaaaggcott caaaactacc ctatttaaaa tagcacctgc
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cactgccate tecataceca ttttcatttt tecatageae ttatecetae ttggcattat
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gttatatatt tgtttatttg kttactgnct gtctccccca ctggactgta agctccatga
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ctgtaagtac atagatgaat tacaaaatga atcaatggng aawtatcctt gmcatatatt
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agtgatatag ttraatotto taaactacat ttttctcatt tcccgattta attaaatcag
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tgatataaaa aaaagagtga tggggatatg tgaaagaaga ccaaaataga tgccaggaaa
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tactaaaact gctgaagttt agtggtatat tttttcttta cacacagtat tatttgagtt
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actaattgtg tcactgaatt acagaataag caaaatacta ggtaaacaga atcacgcttg

ggggctatat tttgtgtaaa atttgtgtta tgcaaaaata atattaaata tttaattact

acagttttgt tatttctttc ttattttagg aaatgatttg cagctgagtg aatcaggaag

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<222> (11)

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<213> Homo sapiens
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                                                                      120
tetgttaeta gagtggagag tetacetteg teteacatgt gecacaaagg atggeatgge
                                                                      180
ccgggagtge cccaccacgt ggetttcacc ccctgcaaag ccagaettcg cccagcgaca
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cagtgtcaag cccacagctc tccaaggagg aagatggtcc aggctgggag catcycctta
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gcagcagcct ctgatccctt ggccaagcag gagggaacca ttagcagcct gaggagctgg
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ctggctggga gcctcgggga ccgcccagec ttgctcccag ctcacccaca agatgtggac
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agotottgtg ctcatttgga ttttytcctt gtccttatct gaaagccatg cggcatccaa
                                                                      480
cgatccacgc aactttgtcc ctaacaaaat gtggaaggga ttagtcaaga ggaatgcatc
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tgtggaaaca gttgataata aaacgtctga ggatgtaacc atggcagcag cttctcctgt
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cacattgacc aaagggattc ggcagcccam ctcaactcta tggaagtcac aacagaggac
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acaagcagga cagatgtgag tgaaccagca acttcaggag gtgcagctga tggtgtgacc
                                                                      720
tecattgete ecaeggetgt ggeetecagt acgaetgegg ectecattac gaetgeggee
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tecagtatga etgtggeete cagtgetece acgaetgeag ectecagtae aactgtggee
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tccattgctc ccacgactac agcctccagt atgactgcgg cctccagcac tcccatgaca
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cttgcactcc ccgcgcccac gtccacttyc acagggcgga ccccgtccac taccgccact
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acagcaacce tggccacatt ggccacacgt gctcagactg tagcgaccac agcaaacaca
                                                                     1080
agcagcccca tgagcactcg tccaagtcct tccaagcaca tgcccagtga caccgcggca
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cagcotgtgg ttaacacaac awataaatco acamcoatgo cotcaaacac aacomowgag
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cccctcaccc aggccgtggt agacaaaact ctccttctgg tggtgctgtt actcggggtg
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accettitea teacagtett ggttttgttt geeetgeagg cetatgagag etacaagaag
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aaggactaca cccaggtgga ctacttaatc aacgggatgt atgcggactc agaaatgtga
                                                                     1440
1500
gaccaaacca agtgetteca aattettttg gtgeaattga ggagatatge cagatgetta
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<222> (9)
<223> n equals a,t,g, or c
<220>
<221> SITE
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<223> n equals a,t,g, or c
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 <223> n equals a,t,g, or c
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                                                                   120
agataagatt aagggctggg tetgtgetea attaacteet gtgggcaegg gggctgggaa
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gagcaaagte ageggtgeet acagteagea ceatgetggg cetgeegtgg aagggaggte
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tgtcctgggc gctgctgctg cttctcttag gctcccagat cctgctgatc tatgcctggc
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atttccacga gcaaagggac tgtgatgaac acaatgtcat ggctcgttac ctccctgcca
                                                                    360
cagtggagtt tgctgtccac acattcaacc aacagagcaa ggactactat gcctacagac
                                                                    420
tggggcacat cttgaattcc tggaaggagc aggtggagtc caagactgta ttctcaatgg
                                                                    480
agetactget ggggagaact aggtgtggga aatttgaaga cgacattgac aactgecatt
                                                                    540
tccaagaaag cacagagctg aacaatactt tcacctgctt cttcaccatc agcaccaggc
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cctggatgae tcagttcage ctcctgaaca agacctgctt ggagggattc cactgagtga
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aacccactca caggettgte catgtgetge teccacatte egtggacate agcactacte
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tyctgaggac tetteagtgg etgageaget ttggaettgt ttgttateet attttgeatg
                                                                    780
tgtttgagat ctcagatcag tgttttagaa aatccacaca tcttgagcct aatcatgtag
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<211> 906
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<221> SITE
<222> (833)
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gatgaggetg etgtgtggcc tgtggetgtg geteteettg etgaaagtee tgcaggeeca
                                                                   240
gaccccaacc cccctgccac tcccgcccc gatgcagagc ttccaaggaa accagttcca
                                                                   300
gggggaatgg ttcgtcctgg gcctggcggg caacagcttc aggccggagc acagggcgct
                                                                   360
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<212> DNA

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gctggaccag ttcatctgcc tgggcagage tcarggecte teggatgaca acattgtett
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                                                                         600
 cccagatgtg actggargtg ccctggacct carcagcctg ccctgggtgg cagcccage
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 ctgaccacte agacageege ggeececaag geetgactet tettgtggga gggegagget
                                                                         720
 ggtcacccca ggccagcgtc tgttgaagga tgaagcagct cctgtccggc ccagcctgc
                                                                         780
 ctcacagetg tgcgagetet gecetectca geteteaaac etgaataaat genecaagee
                                                                         840
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                                                                         900
 agattg
                                                                         906
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 <211> 680
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 <213> Homo sapiens
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                                                                         120
gacetgtggg ccatgatget acceesatgg etgetgetge tgtteettet ettettett
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ctetteetee teaccagggg eteactitet ecaacaaaat acaacettit ggageteaag
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gagtettgea teeggaacca ggaetgegag actggetget gecaaegige teeagacaat
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gagaaatggc ttagcatcgc ctatggccgt tgtcagaaaa ttggaaggca gaagttggct
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aagaaaatgt tettetagtg etceeteett ettgetgset eetcetyety cacetgetet
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cetecetace cagagesetg tgkteaccet gtteeceaga geetecacca tgagtggagg
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aaactcgagg gggggcccgg
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<210> 74
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<213> Homo sapiens
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                                                                              300
 cagteeteet geteetgetg etgegtgeet gggetetggt catgecagge tteettgtgt
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 cotgogtotg tggcoggtto otgocaaco: gtotagtoot ttoaggottg aggcootgoa
                                                                              420
 tigetettic iggicetete coeteettee egeteeceat clageettit itgggiteeg
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                                                                              660
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ctaaggctaa ccaatagaaa tgaacctgtg taatgtccca tgggcataat tcatggagcc
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atetteagga geggeetact agagecacae attteecage teteettgtg tgttteecag
                                                                            1380
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accettette categigies telecetiag geteetggaa agitticaga gagaatease
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cagtggtaac attgttaaac aaaacaggaa aatgggactt gtgtgtatat atgattaaat
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acacactgat gctcaaatcc taaggtgcca agctctaggc cctggaggct ggtagaacag
                                                                             180
gatctatgcc tggaatcctg gcagggattc ctgtcaagga cttgtgttta agcctgcttc
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agggetteag getgettetg etetgtgtet geccaggetg getgageggg tggatgggtg
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gacagaaggg ctcaccaagg attgtggaca tagggtaggc cctggtacca cgggtttcag
                                                                             360
getgttatea ettecettgt aggaacatag ceagaageag atgagecagg gtagaggget
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ggcccctcct ctcatcitce cttcagtctt aaattgtctc cagcgatggg aagaggccag
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agaagtatga tteetetgte tteagtiett tteaggggea teetgeecat agtacceagt
                                                                            900
teccaagggg cececagtea egtggtgaag cetageacte atgeagetet tagggaacea
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                                                                         240
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tgcatacagg tttatatgta ggaaaaattc ctagagtagg attgctggac caatggataa
aagtatattg tggacagaca atgccaaatt gcctttcaga gactgtggcc ctgtgcaccc
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catcaggeat gtgtgactac caaageteet gteagetgtt ttattttate teettteeag
                                                                         480
teteaggete aatgeagaae tttgaggtaa gettttetaa aatgtagget eetaaaegee
                                                                         540
acagecaget etgecacatg aaggagaget caaacgagae agaaacagee tetgggcagg
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                                                                         720
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                                                                         900
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gctactcagg aggctgaggc aggagaatgg cgtgaacctg ggaggtggag gttgcagtga
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1184
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ggtgcatttt gtgtgtgcct tccagagcca gtggactggt gtgtatccaa tgatgccacc
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gcattcacca tgccaatcca aggcagctga tggcttagga aagtcagaga ctgagatgtt
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attccagttg caaaccaatt gtagaatact ataaaaccag agtacaagtc taatagcata
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                                                                                  1260
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/<211> 368
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1140

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aatgggtcc: tctgcattaa aaaagttgat aaagatatag atgttaagct aaaaagcttg

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1841
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gettetteat gtatettat agtatgatet tagetttgat aaatgaetga agetggagaa
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<213> Homo sapiens

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gaacgtgaga gracaatctg gacaggatca gaagtagaga atgaagttgt aagagaaagg
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1020
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gactggctga aggtccgtat gfactcgcgc acagttgcca tcatcggcgg ctttcttgtg
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2214
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<213> Homo sapiens
<400> 114
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  ggcggctgcc tcttgtgctg cggcgcctgg gtctgcaccg gccgtcccga cctcagcttc cccgtgaagt actcagcgcc gcggcggccc acggccaccg gcgactacga caagaagaac
  tacgtetgag ggcgetggge acggccggge ceeteetgee agceaegeet gegaggegtt
  ggataagee: ggggageeee geatggaeeg eggetteege egggtagege ggegegeagg
  ctecteggaa egteeggete tgegeecega egeggeteet ggateegete etgeetgege
  ccgcagctga ccttctcctg ccactagccc ggccctgccc ttaaccagacg gaatgaagtt
tccttttctg tgcgcggcgc tgtttccata ggcagagcgg gtgtcagact gaggatttcg
  cttcccctcc aagacgctgg gggtcttggc tgctgcctta cttcccagag gctcctgctg
 acttoggagg ggcgatgca gagccaggg cccccaccgg aagatgtgta cacctggtct
ttactccatc ggcaggccc gagccaggg accagtgact tggcctggac ctcccggtct
cactccagga tctccccagg caaggcttgt gggcaccgga gcttgagaga gggcgggagt
 gggaaggcta agaatctgct tagtaaatgg tttgaactct сааааааааа аааааааааа
<210> 123
<211> 3793
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<213> Homo sapiens
<220>
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<222> (1102)
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<220>
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<223> n equals a.t.g. or c
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<223> n equals a.t.g. or c
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<222> (3176) <223> n equals a,t,g, or c

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tccacgctag acctgtcaaa tragagaatc tagagattag acctggcgtg tcagcaaggt catccaggaa gcagaagctg agacggagtt aggtgtgatt acttacatag tcgatfacat tttacaaaat acartttata tgtctcattt actgtgcttt ctccctacc catttgtat ctttccttt gctttgctag attgtcaat tttctctctc tttcctgttt ctctctttc aatattcaaa cttctgaaa agtaattcat cataactaaa tatctattgg ggttatgct cacttacaaa cttctgaaaa cggctttact gagatataat tgataattt aagtgtacag tttgttaaa tttgcacata tttaaaatgt ggactttggt aaatgttgac atagtttac actgtgaaa ccatcagcat aatcaagata ataaacttgt ccatcaccc ccaaaaaaaaa aaa													
<210> 124													
<211> 370													
<212> PRT <213> Homo sapiens													
<220>													
<220> <221> SITE													
<222> (370)													
<223> Xaa equals stop translation													
<400> 124													
Met Leu Gly Ala Phe Val Trp Pro Ser Leu Leu Leu Leu Ala Ala													
1 5 10 15													
Cys Ile Cys Leu Leu Thr Phe Ile Asn Cys Ala Tyr Val Lys Trp Gly 20 25 30													
Thr Leu Val Gln Asp Ile Pne Thr Tyr Ala Lys Val Leu Ala Leu Ile 35 40 45													
Ala Val Ile Val Ala Gly Ile Val Arg Leu Gly Gln Gly Ala Ser Thr 50 55 60													
His Phe Glu Asn Ser Phe Glu Gly Ser Ser Phe Ala Val Gly Asp Ile 65 70 75 80													
Ala Leu Ala Leu Tyr Ser Ala Leu Phe Ser Tyr Ser Gly Trp Asp Thr 85 90 95													
Leu Asn Tyr Val Thr Glu Glu Ile Lys Asn Pro Glu Arg Asn Leu Pro 100 105 110													
Leu Ser Ile Gly 11e Ser Met Pro Ile Val Thr Ile Ile Tyr Ile Leu 115 120 125													
Thr Asn Val Ala Tyr Tyr Thr Val Leu Asp Met Arg Asp Ile Leu Ala 130 135 140													
Ser Asp Ala Val Ala Val Thr Phe Ala Asp Gln Ile Phe Gly Ile Phe 145 150 155 160													
Asn Trp Ile Ile Pro Leu Ser Val Ala Leu Ser Cys Phe Gly Gly Leu 165 170 175													
Asn Ala Ser Ile Val Ala Ala Ser Arg Leu Phe Phe Val Gly Ser Arg 180 185 190													
Glu Gly His Leu Pro Asp Ala Ile Cys Met Ile His Val Glu Arg Phe													

195 200 Thr Pro Val Pro Ser Leu Leu Phe Asn Gly Ile Met Ala Leu Ile Tyr Leu Cys Val Glu Asp Ile Phe Gln Leu Ile Asn Tyr Tyr Ser Phe Ser 225 230 235 240 Tyr Trp Phe Phe Val Gly Leu Ser Ile Val Gly Gln Leu Tyr Leu Arg 245 250 255 Trp Lys Glu Pro Asp Arg Pro Arg Pro Leu Lys Leu Ser Val Phe Phe 260 265 270 Pro Ile Val Phe Cys Leu Cys Thr Ile Phe Leu Val Ala Val Pro Leu 275 280 285 Tyr Ser Asp Thr Ile Asn Ser Leu Ile Gly Ile Ala Ile Ala Leu Ser 290 295 300 Gly Leu Pro Phe Tyr Phe Leu Ile Ile Arg Val Pro Glu His Lys Arg 305 310 315 320Pro Leu Tyr Leu Arg Arg Ser Trp Gly Leu Pro Gln Gly Thr Ser Arg 325 330 335 Ser Cys Val Cys Gln Leu Leu Gln Lys Trp Ile Trp Lys Met Glu Glu 340 345 350Arg Cys Pro Ser Asn Gly Ile Pro Ser Leu Thr Lys His His Leu Glu 355 360 365Ser Xaa 370 <210> 125 <211> 86 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (86) <223> Xaa equals stop translation <400> 125 Met Gly Phe Trp Cys Gly Cys Pro Phe Cys Leu Leu Val Val Leu Leu 1 5 10 15 Thr Asp Arg Thr Leu Scr Cys Arg Ser Val Gly Val Pro Cys Asn Val 20 25 36

Arg Cys Gln Cys Ala Pro Ala Gly Gly Cys Leu Pro Val Arg Leu Leu 35 40 45

Ala Gly Gln Gly Ser Gly Thr His Leu Arg Arg Gln Ser Ala Arg Ser 50  $\,$  55  $\,$  60

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Gln Ile Ser Ser Cys Met Leu Gly Glu Pro Leu Leu Ser Ser Lys Leu
  Ser Asp Arg Asp Ile Xaa
                      85
  <210> 126
  <211> 44
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SITE
<222> (44)

<223> Xaa equals stop translation
  Met Tyr Thr Lys Thr His Lys Phe Lys Phe Tyr Asn Phe Leu Ser Leu

1 5 10 15
  Trp Ile Trp Lys Ile Phc Phe Leu Leu Phe Phe Ile Leu Ile Val Ala 20 \hspace{1.5cm} 25 \hspace{1.5cm} 30
  Leu Ala Phe Pro Ile Pro Cys Leu Ser Ile Phe Xaa
 <210> 127
<211> 319
  <212> PRT
  <213> Homo sapiens
  <220>
 <221> SITE <222> (264)
 <223> Xaa equals any of the naturally occurring L-amino acids
  <220>
  <221> SITE
  <222> (303)
 <223> Xaa equals any of the naturally occurring L-amino acids
 <400> 127
 Met Asn Thr Asp His Leu Arg Leu Thr Val Pro Asn Gly Ile Gly Ala

1 5 10 15
 Lcu Lys Leu Arg Glu Met Glu His Tyr Phe Ser Gln Gly Leu Ser Val 20 25 30
 Gln Leu Phe Asn Asp Gly Ser Lys Cly Lys Leu Asn His Leu Cys Gly 35 40 45
 Ala Asp Phe Val Lys Ser His Gln Lys Pro Pro Gln Gly Met Glu Ile
50 55 60
 Lys Ser Asn Glu Arg Cys Cys Ser Phe Asp Gly Asp Ala Asp Arg Ile
65 70 75 80
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WO 00/06698 PCT/US99/17130

Val Tyr Tyr His Asp Ala Asp Gly His Phe His Leu Ile Asp Gly 85 90 95

Asp Lys IIe Ala Thr Leu ile Ser Ser Phe Leu Lys Glu Leu Leu Val 100 105 110

Glu Ile Gly Glu Ser Leu Asn Ile Gly Val Val Gln Thr Ala Tyr Ala 115 120 125

Asn Gly Ser Ser Thr Arg Tyr Leu Glu Glu Val Met Lys Val Pro Val 130 135

Tyr Cys Thr Lys Thr Gly Val Lys His Leu His His Lys Ala Glu 145 150 155 160

Phe Asp Ile Gly Val Tyr Phe Glu Ala Asn Gly His Gly Thr Ala Leu 165 , 170 175

Phe Ser Thr Ala Val Glu Met Lys Ile Lys Gln Ser Ala Glu Gln Leu 180 185 190

Glu Asp Lys Lys Arg Lys Ala Ala Lys Met Leu Glu Asm Ile Ile Asp 195 200 205

Leu Phe Asn Gln Ala Ala Gly Asp Ala Ile Ser Asp Met Leu Val Ile 210 215 220

Glu Ala Ile Leu Ala Leu Lys Gly Leu Thr Val Gln Gln Trp Asp Ala 225 230 235 240

Leu Tyr Thr Asp Leu Pro Asn Arg Cln Leu Lys Val Gln Val Ala Asp 245 250 255

Arg Arg Val Ile Ser Thr Thr Xaa Ala Glu Arg Gln Ala Val Thr Pro 260 265 270

Pro Gly Leu Gln Glu Ala Ile Asn Asp Leu Val Lys Lys Tyr Lys Leu 275 280 285

Ser Arg Ala Phe Val Arg Fro Ser Gly Thr Glu Asp Val Val Xaa Ser 290 295 300

Ile Cys Arg Ser Arg Leu Thr Arg Lys Cys Arg Ser Pro Cys Thr 305  $_{\odot}$  310 315

<210> 128
<211> 46

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> {46}

<223> Xaa equals stop translation

Met Asp Ket Val Cys Phe Cys Ile Tyr Leu Gly Leu Leu Lys Phe Ile 1 5 10 15

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Ser Ala Ile Phe Cys Ser Phe Ser Glu Glu Val Leu Tyr Ile Ser Phe
              20
Val Lys Cys Ile Pro Lys Tyr Phe Val Glu Met Leu Leu Xaa
         35
                              40
<210> 129
<211> 709
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (189)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (275)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (414)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (438)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (641)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (643)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (696)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (697)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 129
Met Ala Gly Leu Asn Cys Gly Val Ser Ile Ala Leu Leu Gly Val Leu
                                     10
Leu Leu Gly Ala Ala Arg Leu Pro Arg Gly Ala Glu Ala Phe Glu Ile
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Ala Leu Pro Arg Glu Ser Asn Ile Thr Val Leu Ile Lys Leu Gly Thr 35 40 45 Pro Thr Leu Leu Ala Lys Pro Cys Tyr Ile Val Ile Ser Lys Arg His 50 55 6011e Thr Met Leu Ser Ile Lys Ser Gly Glu Arg Ile Val Phe Thr Phe
65 70 75 80 Ser Cys Gln Ser Pro Glu Asn His Phe Val Ile Glu Ile Gln Lys Asn 85 90 95 Ile Asp Cys Met Ser Gly Pro Cys Pro Phe Gly Glu Val Gln Leu Gln 100 105 110 Pro Ser Thr Ser Leu Leu Pro Thr Leu Asn Arg Thr Phe Ile Trp Asp 115 120 125 Val Lys Ala His Lys Ser Ile Gly Leu Glu Leu Gln Phe Ser Ile Pro 130 135 140 Arg Leu Arg Gln Ile Gly Pro Gly Glu Ser Cys Pro Asp Gly Val Thr 145 150 155 160 His Ser Ile Ser Gly Arg Ile Asp Ala Thr Val Val Arg Ile Gly Thr 165 170 175 Phe Cys Ser Asn Gly Thr Val Ser Arg Ile Lys Met Xaa Glu Gly Val Lys Met Ala Leu His Leu Pro Trp Phe His Pro Arg Asn Val Ser Gly 195 200 205 Phe Ser Ile Ala Asn Arg Ser Ser Ile Lys Arg Leu Cys Ile Ile Glu 210 215 220 Ser Val Phe Glu Gly Glu Gly Ser Ala Thr Leu Met Ser Ala Asn Tyr 225  $230 \hspace{1.5cm} 230 \hspace{1.5cm} 235 \hspace{1.5cm} 240$ Pro Glu Gly Phe Pro Glu Asp Glu Leu Met Thr Trp Glr Phe Val Val 245 250 255 Pro Ala His Leu Arg Ala Ser Val Ser Phe Leu Asn Phe Asn Leu Ser 260 265 270 Asn Cys Xaa Arg Lys Glu Glu Arg Val Glu Tyr Tyr Ile Pro Gly Ser 275 280 285 Thr Thr Asn Pro Glu Val Phe Lys Leu Glu Asp Lys Gln Pro Gly Asn 290 295 300 Met Ala Gly Asn Phe Asn Leu Ser Leu Gln Gly Cys Asp Gln Asp Ala 305 316 315 320 Gln Ser Pro Gly Ile Leu Arg Leu Gir Phe Gln Val Leu Val Gln His 325 330 335

Pro Gln Asn Glu Sor Asn Lys Ile Tyr Val Val Asp Leu Ser Asn Glu

			340					345	5				350	)	
Arg	Ala	Met 355	Ser	Leu	Thx	Ile	: Glu 360	Pro	Arg	Pro	Val	Lys 365		Ser	Ar
Lys	Phe 370	Val	Pro	Gly	Суз	Phe 375	Val	Cys	Leu	Glu	Ser 380		Thr	Cys	Sei
Ser 395	Asn	Leu	Thr	Leu	Thr 390	Ser	Gly	Ser	Lys	His 395		Ile	Ser	Phe	Le: 400
Cys	Asp	Asp	Leu	Thr 405	Arg	гел	Trp	Met	410		Glu	Lys	Xaa	1le 415	
Cys	Thr	Asp	His 420	Arg	Tyr	Cys	Gln	Arg 425		Ser	Туг	Ser	Leu 430		. Val
Pro	Ser	Asp 435	Ile	Leu	Xaa	Leu	Pro 440	Val	Glu	Leu	His	Asp 445		Ser	Trp
Lys	Leu 450	Leu	Val	Pro	Lys	Asp 455	Arg	Leu	Ser	Leu	Val 460	Leu	Val	Pro	Ala
Gln 465	Lys	Leu	Gln	Gln	His 470	Thr	His	Glu	Lys	Pro <b>47</b> 5	Cys	Asn	Thr	Ser	Phe 480
				Ala 485					490					495	
			500	Gly				505					510		
		515		Leu			520					525			•
	530			Leu		535					540				
545				Val	550					555					560
				Asp 565					57C					575	
	٠		580	Pro				585					590		
		595		Val			600					605			
Gln	Glu 610	Gln	Arg	Thr	Arg	Ala 615	Glu	Glu	Ile	Phe	Ser 620	Leu	Asp	Glu	Asp
Val 525	Leu	Pro	Lys	Pro	Ser <b>6</b> 30	Phe	His	His	His	Ser 635	Phe	Ттр	Val	Asn	11e 640
Xaa	Asn	Xaa	Ser	Pro 645	Thr	Ser	Gly	Lys	Gln 650	Leu	Asp	Leu	Leu	Phe 655	Ser

Val Thr Leu Thr Pro Arg Thr Val Asp Leu Thr Val Ile Leu Ile Ala 660 670 .

Ala Val Gly Gly Gly Val Leu Leu Leu Ser Ala Leu Gly Leu Ile Ile 675 680 685

Cys Cys Val Lys Lys Lys Lys Xaa Xaa Thr Arg Gly Pro Ala Val Gly 690 695 700

Ile Tyr Asn Gly Asn 705

<210> 130

<211> 415 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (415)

<223> Xaa equals stop translation

<400> 130

Met Thr Lys Ala Arg Leu Phe Arg Leu Trp Leu Val Leu Gly Ser Val 1 5 10 15

Phe Met Ile Leu Leu Ile Ile Val Tyr Trp Asp Ser Ala Gly Ala Ala , 20 25 30

His Phe Tyr Leu His Thr Ser Phe Scr Arg Pro His Thr Gly Pro Pro 35 40 45

Leu Pro Thr Pro Gly Pro Asp Arg Asp Arg Glu Leu Thr Ala Asp Ser 50 60

Asp Val Asp Glu Phe Leu Asp Lys Phe Leu Ser Ala Gly Val Lys Gln 65 70 75 80

Ser Asp Leu Pro Arg Lys Glu Thr Glu Gln Pro Pro Ala Pro Gly Ser 85 90 95

Met Glu Glu Asn Val Arg Gly Tyr Asp Trp Ser Pro Arg Asp Ala Arg

Arg Ser Pro Asp Gln Gly Arg Gln Gln Ala Glu Arg Arg Ser Val Leu 115 120 125

Arg Gly Phe Cys Ala Asn Ser Ser Leu Ala Phe Pro Thr Lys Glu Arg 130 135 140

Ala Phe Asp Asp Ile Pro Asm Ser Glu Leu Ser His Leu Ile Val Asp 145 150 155 160

Asp Arg His Gly Ala Ile Tyr Cys Tyr Val Pro Lys Val Ala Cys Thr 165 . 170 170 175

Asn Trp Lys Arg Val Net Ile Val Leu Ser Gly Ser Leu Leu His Arg

Gly Ala Pro Tyr Arg Asp Pro Leu Arg Ile Pro Arg Glu His Val His 195 200 205

Asn Ala Ser Ala His Leu Thr Phe Asn Lys Phe Trp Arg Arg Tyr Gly 210 215 220

Lys Leu Ser Arg His Leu Met Lys Val Lys Leu Lys Lys Tyr Thr Lys 225 230 235 240

Phe Leu Phe Val Arg Asp Pro Phe Val Arg Leu Ile Ser Ala Phe Arg 245 250 255

Ser Lys Phe Glu Leu Glu Asn Glu Glu Phe Tyr Arg Lys Phe Ala Val 260 265 270

Pro Met Leu Arg Leu Tyr/Ala Asn His Thr Ser Leu Pro Ala Ser Ala 275 280 285

Arg Glu Ala Phe Arg Ala Gly Leu Lys Val Ser Phe Ala Asn Phe Ile 290 295 300

Gln Tyr Leu Leu Asp Pro His Thr Glu Lys Leu Ala Pro Phe Asn Glu 305 310 315 320

His Trp Arg Gln Val Tyr Arg Leu Cys His Pro Cys Gln Ile Asp Tyr 325 330 335

Asp Phe Val Gly Lys Leu Glu Thr Leu Asp Glu Asp Ala Ala Gln Leu 340 345 350

Leu Gln Leu Leu Gln Val Asp Arg Gln Leu Arg Phe Pro Pro Ser Tyr 355 360 365

Arg Asn Arg Thr Ala Ser Ser Trp Glu Glu Asp Trp Phe Ala Lys Ile  $370 \hspace{1cm} 375 \hspace{1cm} 380 \hspace{1cm}$ 

Pro Leu Ala Trp Arg Gln Gln Leu Tyr Lys Leu Tyr Glu Ala Asp Phe 385 390 395 400

Val Leu Phe Gly Tyr Pro Lys Pro Glu Asn Leu Leu Arg Asp Xaa 405 410 410

<210> 131

<211> 212

<212> PRT

<213> Homo sapiens

<400> 131

Met Gln Leu Gly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly Cys

1 5 10 15

Phe Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg Lys 20 25 30

Pro Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala Val 35 40 45

Leu Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe Ala 50 60

Leu Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr Ile 65 70 75 80

Gly Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr Ser 85 90 95

Arg Thr Val Ala Ile Ile Gly Gly Phe Leu Val Leu Ala Ser Gly Ala 100 105 110

Gly Gln Val Phe Leu Gly Ile Tyr Leu Ile Cys Val Ala Tyr Ser Leu 130 135 140

Gln His Ser Lys Glu Asp Arg Leu Ala Tyr Leu Asn His Leu Pro Gly 145 150 155 160

Gly Glu Leu Met Ile Gln Leu Phe Phe Val Leu Tyr Gly Ile Leu Ala 165 170 175

Leu Ala Phe Leu Ser Gly Tyr Tyr Val Thr Leu Ala Ala Gln Ile Leu 180 185 190

Ala Val Leu Leu Pro Pro Val Met Leu Leu Ile Asp Gly Asn Val Ala 195 200 205

Tyr Trp His Asn Thr Arg Arg Val Glu Phe Trp Asn Gln Met Lys Leu 210 215 220

Leu Gly Glu Ser Val Gly Ile Phe Gly Thr Ala Val Ile Leu Ala Thr 225 235 240

Asp Gly

<210> 132

<211> 313

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (313)

<223> Xaa equals stop translation

<400> 132

Met Glu Ser Leu Tyr Asp Leu Trp Glu Phe Tyr Leu Pro Tyr Leu Tyr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Ser Cys Ile Ser Leu Met Gly Cys Leu Leu Leu Leu Cys Thr Pro 20 25 30

Val Gly Leu Ser Arg Met Phe Thr Val Met Gly His Leu Leu Val Lys 35 40 45

- Pro Thr Ile Leu Glu Asp Leu Asp Glu Gln Ile Tyr Ile Ile Thr Lèu 50 55 60
- Glu Glu Glu Ala Leu Gln Arg Arg Leu Asn Gly Leu Ser Ser Ser Val 65 70 75 80
- Glu Tyr Asn Ile Met Glu Leu Glu Glu Glu Leu Glu Asn Val Lys Thr 85 90 95
- Leu Lys Thr Lys Leu Glu Arg Arg Lys Lys Ala Ser Ala Trp Glu Arg 100 105 110
- Asn Leu Val Tyr Pro Ala Val Met Val Leu Leu Leu Ile Glu Thr Ser 115 120 125
- Ile Ser Val Leu Leu Val Ala Cys Asn Ile Leu Cys Leu Leu Val Asp 130 135 140
- Glu Thr Ala Met Pro Lys Gly Thr Arg Gly Pro Gly Ile Gly Asn Ala 145 150 155 160
- Ser Leu Ser Thr Phe Gly Phe Val Gly Ala Ala Leu Glu Ile Ile Leu 165 170 175
- Ile Phe Tyr Leu Met Val Ser Ser Val Val Gly Phe Tyr Ser Leu Arg 180 185 190
- Phe Phe Gly Asn Phe Thr Pro Lys Lys Asp Asp Thr Thr Met Thr Lys 195 200 205
- Ile Ile Gly Asn Cys Val Ser Ile Leu Val Leu Ser Ser Ala Leu Pro 210 215 220
- Val Met Ser Arg Thr Leu Gly Ile Thr Arg Phe Asp Leu Gly Asp 225 230 235 240
- Phe Gly Arg Phe Asn Trp Leu Gly Asn Phe Tyr Ile Val Leu Ser Tyr 245 250 255
- Asn Leu Leu Phe Ala Ile Val Thr Thr Leu Cys Leu Val Arg Lys Phe 260 265 270
- Thr Ser Ala Val Arg Glu Glu Leu Phe Lys Ala Leu Gly Leu His Lys 275 280 285
- Leu His Leu Pro Asn Thr Ser Arg Asp Ser Glu Thr Ala Lys Pro Ser 290 295 300
- Val Asn Gly His Gln Lys Ala Leu Xaa 305 310
- <210> 133
- <211> 183
- <212> PRT
- <213> Homo sapiens

<220>

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<221> SITE
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<222> (183) <223> Xaa equals stop translation

<400> 133

Met Met Val Cys Ser Ile Met Met Tyr Phe Leu Leu Gly Ile Thr Leu 1 5 10 15

Leu Leu Asn Ala Ser Ile Thr Glu Thr Phe Asr. Cys Ser Phe Ser Cys 35 40 45

Gly Pro Asp Cys Trp Lys Leu Ser Gln Tyr Pro Cys Leu Gln Val Tyr 50 60

Val Asn Leu Thr Ser Ser Gly Glu Lys Leu Leu Tyr His Thr Glu 65 70 75 80

Glu Thr Ile Lys Ile Asn Gln Lys Cys Ser Tyr Ile Pro Lys Cys Gly 85 90 95

Lys Asn Phe Glu Glu Ser Met Ser Leu Val Asn Val Val Met Glu Asn 100 105 110

Phe Arg Lys Tyr Gln His Phe Ser Cys Tyr Ser Asp Pro Glu Gly Asn 115 120 125

Gln Lys Ser Val Ile Leu Thr Lys Leu Tyr Ser Ser Asn Val Leu Phe 130 135 140

His Ser Leu Phe Trp Pro Thr Cys Met Met Ala Gly Gly Val Ala Ile 145 150 150 160

Val Ala Met Val Lys Leu Thr Glr. Tyr Leu Ser Leu Leu Cys Glu Arg 165 170 175

Ile Gln Arg Ile Asn Arg Xaa 180

<210> 134

<211> 147

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (147)

<223> Xaa equals stop translation

<400> 134

Met Trp Lys Leu Trp Arg Ala Glu Glu Gly Ala Ala Ala Leu Gly Gly

1 5 10 15

Gln Arg Arg Pro Net Gly Phe Pro Pro Gly Pro Pro Gly Leu Pro Phe 35

Ile Gly Asn Ile Tyr Ser Leu Ala Ala Ser Ser Glu Leu Pro His Val

Tyr Met Arg Lys Gln Ser Gln Val Tyr Gly Glu Val Gln Pro Arg Arg 65 70 75 80

Ala Pro Gly Arg Glu Gly Arg Gln Ala Gly Pro Gly Trp Pro Gly Pro 85 90 95

Ser Trp Leu Asp Leu Trp Pro Pro Leu Gly Arg Leu Val Gly Thr Ser

Pro Cys Ala Gly Cys Pro Leu Arg Asp Thr Arg Phe Pro Cly Leu Glu 115 g<sup>3</sup> 120 125

Gly Arg Ser Pro Arg Arg Ala Pro Leu Gln Gly Glu Pro Arg Pro 130 135 140

Cys Arg Xaa 145

<210> 135

<211> 122

<212> PRT

<213> Homo sapiens

<400> 135

Net Arg Val Arg Ile Gly Leu Thr Leu Leu Leu Cys Ala Val Leu Leu 1 5 10 15

Leu Asp Ser Lys Thr Thr Leu Thr Ser Asp Glu Ser Val Lys Asp His  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Thr Thr Ala Gly Arg Val Val Ala Gly Gin Ile Phe Leu Asp Ser Glu  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Glu Ser Glu Leu Glu Ser Ser Ile Gln Glu Glu Glu Asp Ser Leu Lys 65 70 75 80

Ser Gln Glu Gly Glu Ser Val Thr Glu Asp Ile Ser Phe Leu Glu Ser 85 90 95

Pro Asn Pro Glu Asn Lys Asp Tyr Glu Glu Pro Lys Lys Val Arg Lys 100 105 110

Pro Gly Ser Leu Asp Ile Phe Leu Ala Phe 115 120

<210> 136

<211> 112

<212> PRT

<213> Homo sapiers

Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly
1 5 10 15

Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly 20 25 30

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys 35 40 45

Cys Met Asp Cys Ser Thr Ser Cys Pro Leu Pro Ala Ala Leu Ala His 50 55 60

Pro Trp Gly Arg Ser Glu Pro Asp Leu Arg Ala Gly Ala Ala Phe Trp 65 70 75 80

Leu Phe Gly Leu Glu Thr Met Pro Gln Arg Glu Lys Phe Thr Thr Pro 85 90 95

Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu lle Gln
100 105 110

<210> 137

<211> 140 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (140)

<223> Xaa equals stop translation

<400> 137

Met Leu Leu Gly Pro Val Pro Ile Leu His Ile Lys Ser Gln Leu Trp
1 5 10 15

Leu Leu Val Leu Ile Leu Val Val Ser Gly Leu Ser Ala Gly Met Ser 20 25 30

Ile Ile Pro Thr Phe Pro Clu Ile Leu Ser Cys Ala His Glu Asn Gly 35 40 . . . 45

Phe Glu Glu Gly Leu Ser Thr Leu Gly Leu Val Ser Gly Leu Phe Ser 50 60

Ala Met Trp Ser Ile Gly Ala Phe Met Gly Pro Thr Leu Gly Gly Phe 65 70 75 80

Leu Tyr Glu Lys Ile Gly Phe Glu Trp Ala Ala Ala Ile Gln Gly Leu 85 90 95

Trp Ala Leu Ile Ser Gly Leu Ala Met Gly Leu Phe Tyr Leu Leu Glu 100 105 110

Tyr Ser Arg Arg Lys Arg Ser Lys Ser Gln Asn Ile Leu Ser Thr Glu 115 120 125

Glu Glu Arg Thr Thr Leu Leu Pro Asn Glu Thr Xaa

<210> 138

<211> 404 <212> PRT

<213> Homo sapiens

Met Arg Leu Gln Asp Val Tyr Met Leu Asn Val Lys Gly Leu Ala Arg

1 5 10 15

Gly Val Phe Gln Arg Val Thr Gly Ser Ala Ile Thr Asp Leu Tyr Ser 20 25 30

Pro Lys Arg Leu Phe Ser Leu Thr Gly Asp Asp Cys Phe Gln Val Gly  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Lys Val Ala Tyr Asp Met Gly Asp Tyr Tyr His Ala Ile Pro Trp Leu 50 60

Glu Glu Ala Val Ser Leu Phe Arg Gly Ser Tyr Gly Glu Trp Lys Thr 65 70 75 80

Glu Asp Glu Ala Ser Leu Glu Asp Ala Leu Asp His Leu Ala Phe Ala 85 90 95

Tyr Phe Arg Ala Gly Asn Val Ser Cys Ala Leu Ser Leu Ser Arg Glu 100 105 110

Phe Leu Leu Tyr Ser Pro Asp Asn Lys Arg Met Ala Arg Asn Val Leu 115 120 125.

Lys Tyr Glu Arg Leu Leu Ala Glu Ser Pro Asn His Val Val Ala Glu 130 135 140

Ala Val Ile Gln Arg Pro Asn Ile Pro His Leu Gln Thr Arg Asp Thr 145 150 155 160

Tyr Glu Gly Leu Cys Gln Thr Leu Gly Ser Gln Pro Thr Leu Tyr Gln 165 170 175

Ile Pro Ser Leu Tyr Cys Ser Tyr Glu Thr Asn Ser Asn Ala Tyr Leu 180 185 190

Leu Leu Glu Pro Ile Arg Lys Glu Val Ile His Leu Glu Pro Tyr Ile 195 200 205

Ala Leu Tyr His Asp Phe Val Ser Asp Ser Glu Ala Gln Lys Ile Arg 210 215 220

Glu Leu Ala Glu Pro Trp Leu Gln Arg Ser Val Val Ala Ser Gly Glu 225 230 235 240

Lys Gln Leu Gln Val Glu Tyr Arg Ile Ser Lys Scr Ala Trp Leu Lys 245 250 255

Asp Thr Val Asp Leu Lys Leu Val Thr Leu Asn His Arg Ile Ala Ala 260 265 270

Leu Thr Gly Leu Asp Val Arg Pro Pro Tyr Ala Glu Tyr Leu Gln Val 275 280 285

Val Asn Tyr Gly Ile Gly Gly His Tyr Glu Pro His Phe Asp His Ala 290 . 295 300

Thr Ser Pro Ser Ser Pro Leu Tyr Arg Met Lys Ser Gly Asn Arg Val 305

Ala Thr Phe Met Ile Tyr Leu Ser Ser Val Glu Ala Gly Gly Ala Thr 325  $\ensuremath{\circ}$  330 335

Ala Phe Ile Tyr Ala Asn Leu Ser Val Pro Val Val Arg Asn Ala Ala 340 345 350

Leu Phe Trp Trp Asn Leu His Arg Ser Gly Glu Gly Asp Ser Asp Thr 355 . 360 . 365

Leu His Ala Gly Cys Pro Val Leu Val Gly Asp Lys Trp Val Ala Asn 370 375 380

Lys Trp Ile His Glu Tyr Gly Gln Glu Phe Arg Arg Pro Cys Ser Ser 385 390 395 400

Ser Pro Glu Asp

<210> 139

<211> 96

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (96)

<223> Xaa equals stop translation

<400> 139

Met Lys Ala Pro His Thr Gly Val Leu His Leu Gly Ser Val Trp Val

1 5 10 15

Phe Leu Gly Pro Phe Leu Leu Gly Val Gly Tyr Thr Leu Thr Phe Asn 20 25 30

Prc Leu Ser Gly Cys Met Ser Thr Val Arg Trp Leu Asn Ser Asn Ile  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Thr Ala Asn Arg Thr Leu Ser Arg Ser Val Cys His Val Thr Pro Leu 50 55 . 60

His Arg Ser Leu Ser Pro His Asp Gly Glu Tyr Leu Arg Gln Met Leu 65 70 75 80 Leu Asn Ser Ser Ser Arg Ala Gly Glu Ala Gly Ser Trp Gly Tyr Xaa 85 90 95

<210> 140 <211> 240 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (240) <223> Xaa equals stop translation <400> 140 Met Gly Ser Cys Ala Arg Leu Leu Leu Trp Gly Cys Thr Val Val

1 5 10 15 Ala Ala Gly Leu Ser Gly Val Ala Gly Val Ser Ser Arg Cys Glu Lys 20 25 30Ala Cys Asn Pro Arg Met Gly Asn Leu Ala Leu Gly Arg Lys Leu Trp  $35 \hspace{1cm} 40 \hspace{1cm} 45$ Ala Asp Thr Thr Cys Gly Gln Asn Ala Thr Glu Leu Tyr Cys Phe Tyr 50 55 60 Ser Glu Asn Thr Asp Leu Thr Cys Arg Gln Pro Lys Cys Asp Lys Cys 65 70 75 80 Asn Ala Ala Tyr Pro His Leu Ala His Leu Pro Ser Ala Met Ala Asp 85 90 95 Ser Ser Phe Arg Phe Pro Arg Thr Trp Trp Gln Ser Ala Glu Asp Val 100 100 105 110His Arg Glu Lys Ile Gln Leu Asp Leu Glu Ala Glu Phe Tyr Phe Thr 115 120 125 His Leu Ile Val Met Phe Lys Ser Pro Arg Pro Ala Ala Met Val Leu 130 135 140 Asp Arg Ser Gln Asp Phe Gly Lys Thr Trp Lys Pro Tyr Lys Tyr Phe 145 150 155 160 Ala Thr Asn Cys Ser Ala Thr Phe Gly Leu Glu Asp Asp Val Val Lys 165 170 175 Lys Gly Ala Ile Cys Thr Ser Lys Tyr Ser Ser Pro Phe Pro Cys Thr Gly Arg Lys Val Ile Phe Lys Ala Leu Ser Pro Pro Tyr Asp Thr Glu 195 200 205

Asn Pro Tyr Ser Ala Lys Val Gln Glu Gln Leu Lys Ile Thr Asn Leu

J

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210
                             215
                                                    220
 Pro Arg Ala Ala Glu Thr Thr Val Leu Ser Leu Ser Glu Lys Xaa
                                               235
                                                                      240
 <210> 141
<211> 54
 <212> PRT
 <213> Homo sapiens
 <220>
<221> SITE
 <222> (54)
 <223> Xaa equals stop translation
 <400> 141
Met Met Ile Ser Gly Leu Lys Leu Leu Val Leu Phe Leu Lys Phe Ala
1 5 10 15
Pro Glu Asn Tyr Cys Leu Ser Thr Glu Thr Leu Gln Met Pro Asn Arg 20 25 30
His Leu Arg Leu Ser Lys Ala Thr Cys Tyr Leu Mct Lys Cys Leu Leu 35 \hspace{1.5cm} 40 \hspace{1.5cm} 45
Pro Ser Tyr Phe Glu Xaa
50
<210> 142
<211> 67
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<221> G7)
<222> (67)
<223> Xaa equals stop translation
<400> 142
Met Arg Ser Leu Ile Ser Ser His Pro Cys Gln His Leu Leu Leu Leu 1 5 10 15
Leu Leu Leu Phe Leu Ile Leu Ala Ile Leu Val Asp Val Lys Trp 20 25 30
Tyr Leu Val Leu Phe Ile Cys Ile Ser Leu Met Thr Ser Asp Val Glu
His Leu Phe Met Cys Leu Leu Ala Ile Arg Ile Ser Ser Trp Arg Asn 50 55 60
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Val Tyr Xaa

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<210> 143
 <211> 108
 <212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids
<221> SITE
<222> (55)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (58)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (67)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 143
Met Phe Tyr Lys Leu Thr Leu Ile Leu Cys Glu Leu Ser Val Ala Gly
1 5 10 15
Val Thr Gln Ala Ala Ser Gln Arg Pro Leu Gln Arg Leu Pro Arg His 20 25 30
Ile Cys Ser Glm Arg Asn Pro Pro Gly Arg Cys Leu Leu Lys Ala Xaa
                               40
Leu Gln Thr Thr Trp Gly Xaa Pro Asp Xaa Gln Phe Pro Gly Cys Pro
His Pro Xaa Arg Val Thr Leu Asn Ala Arg Gln Met Gly Asn Gly Lys
Glu Lys Lys Ala Ala Asp Leu Lys Leu Lys Phe Pro Gln Lys Arg Phe 85 90 95
Tyr Leu Ser Ala Phe Ser Glu Arg Ile Lys Ala Phe 100 \hspace{1cm} 105 \hspace{1cm}
<210> 144
<211> 84
<212> PRT
<213> Homo sapiers
<220>
<221> SITE
<222> (84)
<223> Xaa equals stop translation
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Leu Gly Trp Thr Gly Leu Ser Trp Val Val His Phe Gly Ala Ser Ala 50 60

Val Met Gly Arg Gln Trp Leu Gly Ser Leu Gln Arg Leu Pro Cys Ile 65 70 75 80

Ser Gly Ser Kaa

<210> 145 <211> 166 <212> PRT <213> Homo sapiens

. . .

Met Gly Ser Arg Phc Leu Leu Val Leu Leu Ser Gly Leu Thr Val Leu

1 5 10 15

Leu Ala Leu Pro Gly Ser Glu Ala Lys Asn Ser Gly Ala Ser Cys Pro 20 25 30

Pro Cys Pro Lys Tyr Ala Ser Cys His Asn Ser Thr His Cys Thr Cys
35 40 45

Glu Asp Gly Phe Arg Ala Arg Ser Gly Arg Thr Tyr Phe His Asp Ser 50 55 60

Ser Glu Lys Cys Glu Asp Tle Asp Gly Cys Gly Thr Gly Loy Ala Lys

Ser Glu Lys Cys Glu Asp Ile Asn Glu Cys Glu Thr Gly Leu Ala Lys 65 70 75 80

Cys Lys Tyr Lys Ala Tyr Cys Arg Asn Lys Val Gly Gly Tyr Ile Cys 85 90 95

Ser Cys Leu Val Lys Tyr Thr Leu Phe Asn Phe Leu Ala Gly Ile Ile 100 105 110

Asp Tyr Asp His Pro Asp Cys Tyr G.u Asn Asn Ser Gln Gly Thr Thr
115 120 125

Gln Ser Asn Val Asp Ile Trp Val Ser Gly Val Lys Pro Gly Phe Gly
130 135 140

Lys Gln Leu Val Arg Ile Thr Met Pro Phe Ser Tyr Pro Asn Ile Asn 145 150 155 160

Met Ser Ser Cys Asp Phe 165

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<210> 146
<211> 70
<212> PRT
 <213> Homo sapiens
 <400> 146
 Met Lys Pro Lys His Leu Glu Trp Cys Leu Ala His Ser Trp Cys Val
1 5 10 15
 Ile Trp Leu Ser Phe Val Ser Pro Pro Thr Ser His Leu Glu Cys Asp
 Gly Phe Pro Gly Ser Leu Leu Pro Pro Cys Glu Glu Gly Arg Cys Phe 35 40 45
 Pro Phe Thr Phe His His His Asp Cys His Gly Cys Ser Pro Leu Gln 50 60
 Ser Ser Pro Gly Gin His
 <210> 147
 <211> 412
 <212> PRT
 <213> Homo sapiens
Met Cys Cys Trp Pro Leu Leu Leu Leu Trp Gly Leu Leu Pro Gly Thr
1 5 10 15
Ala Ala Gly Gly Ser Gly Arg Thr Tyr Pro His Arg Thr Leu Leu Asp 20 25 30
Ser Glu Gly Lys Tyr Trp Leu Gly Trp Ser Gln Arg Gly Ser Gln Ile 35 40 45
Ala Phe Arg Leu Gln Val Arg Thr Ala Gly Tyr Val Gly Phe Gly Phe 50 . 55 60
Ser Pro Thr Gly Ala Met Ala Ser Ala Asp Ile Val Val Gly Gly Val 65 70 75 80
Ala His Gly Arg Pro Tyr Leu Gln Asp Tyr Phe Thr Asn Ala Asn Arg
85 90 95
Glu Leu Lys Lys Asp Ala Gln Gln Asp Tyr His Leu Glu Tyr Ala Met 100 105 110
Glu Asn Ser Thr His Thr Ile Ile Clu Phe Thr Arg Glu Leu His Thr
115 120 175
Cys Asp Ile Asn Asp Lys Ser Ile Thr Asp Ser Thr Val Arg Val Ile
130 135 140
```

Trp Ala Tyr His His Glu Asp Ala Gly Glu Ala Gly Pro Lys Tyr His

- Asp Ser Asn Arg Gly Thr Lys Ser Leu Arg Leu Leu Asn Pro Glu Lys 165 170 175 .
- Thr Ser Val Leu Ser Thr Ala Leu Pro Tyr Phe Asp Leu Val Asn Gln 180 185 190
- Asp Val Pro Ile Pro Asn Lys Asp Thr Thr Tyr Trp Cys Gln Met Phe 195 200 205
- Lys Ile Pro Val Phe Gln Glu Lys His His Val Ile Lys Val Glu Pro 210 215 220
- Val Ile Gln Arg Gly His Glu Ser Leu Val His His Ile Leu Leu Tyr 225 230 235 240
- Gln Cys Ser Asn Asn Phe Asn Asp Ser Val Leu Glu Ser Gly His Glu 245 250 255
- Cys Tyr His Pro Asn Met Pro Asp Ala Phe Leu Thr Cys Glu Thr Val 260 265 270
- Ile Phe Ala Trp Ala Ile Gly Gly Glu Gly Phe Scr Tyr Pro Pro His 275 280 285
- Val Gly Leu Ser Leu Gly Thr Pro Leu Asp Pro His Tyr Val Leu Leu 290 295 300
- Glu Val His Tyr Asp Asn Pro Thr Tyr Glu Glu Gly Leu Ile Asp Asn 305 310 315 320
- Ser Gly Leu Arg Leu Phe Tyr Thr Met Asp Ile Arg Lys Tyr Asp Ala 325 330 335
- Pro Gly Met Pro Glu Phe Gln Ser Glu Gly His Cys Thr Leu Glu Cys 355 360 365
- Leu Glu Glu Leu Trp Lys Pro Lys Ser Gln Val Glu Phe Met Cys Leu 370 375 380
- Leu Phe Phe Ser Met Leu Thr Trp Leu Ala Glu His Gln Ala Ala Ser 385 390 395 400
- Phe Ser Lys Arg Glu Gly Asn Glu Ile Thr Cys Leu 405 410
- <210> 148
- <211> 85
- <212> PRT
- <213> Homo sapiens
- <220>
- <221> SITE
- <222> (85)
- <223> Xaa equals stop translation

<400> 148
Met Asn Val Phe Leu 5
Fro Ala Leu Gly Thr Trp Cly Val Ala Arg 15
Phe Phe Pro His Leu Val Pro Glu Arg Trp Cys Leu Val Phe Cys Cys 25
Trp Ile Phe Phe Phe Phe Phe Phe Phe Phe Phe Cys Thr Lys Val Ala Thr Arg 45
Ser Val Leu Gly Asp Gln Ala Gly Leu Gly Val Gly Cly Pro His Leu 50

Pro Leu Pro Gly Ser His Ser Val Ser Val Pro Glu Lys Thr Ile Phe 65 70 75 80

Ser Leu Lys Gln Xaa 85

<210> 149 <211> 154 <212> PRT <213> Homo sapiens <220>

<221> SITE

<222> (154) <223> Xaa equals stop translation

<400> 149
Met Gly Arg Leu Pro Leu Leu Arg Arg Val Leu Lys Gly Leu Gln Leu
1 5 10 15

Leu Leu Ser Leu Leu Ala Phe Ile Cys Glu Glu Val Val Ser Gln Cys
20 25 30

Thr Leu Cys Gly Gly Leu Tyr Phe Phe Glu Phe Val Ser Cys Ser Ala  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Phe Leu Leu Ser Leu Leu Ile Leu Ile Val Tyr Cys Thr Pro Phe Tyr 50 60

Glu Arg Val Asp Thr Thr Lys Val Lys Ser Ser Asp Phe Tyr Ile Thr 65 70 75 80

Leu Gly Thr Gly Cys Val Phe Leu Leu Ala Ser Ile Ile Phe Val Ser 85 90 95

Thr His Asp Arg Thr Ser Ala Glu Ile Ala Ala Ile Val Phe Gly Phe 100 105 110

Ile Ala Ser Phe Met Phe Leu Leu Asp Phe Ile Thr Mct Leu Tyr Glu 115 120 125

Lys Arg Gln Glu Ser Gln Leu Arg Lys Pro Glu Asn Thr Thr Arg Ala 130  $$135\$ 

Glu Ala Leu Thr Glu Pro Leu Asn Ala Xaa .

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145
                       150
 <210> 150
 <211> 130
 <212> PRT
 <213> Homo sapiens
<220>
<221> SITE
<222> (130)
<223> Xaa equals stop translation
<400> 150
Met Arg Gly His Leu Ala Gly Phe Pro Ala Leu Ser Gly Leu Ala Ser
1 5 10 15
Val Cys Leu Trp Ala Thr Phe Ser Ala Gln Leu Pro Gly Pro Val Ala 20 25 30
Ala Thr Ser Trp Thr Pro Ala Pro Leu Gly Cys Ser Ala Ala Arg Ser 35 40 45
Gly Pro Glu Lys Arg Leu Gly Thr Ala Ala Pro Gly Ser Ala Ala Ser 50 60
Leu Ala Gln Ala Gly Pro Gly Ala Pro Cys Arg Val Leu Pro Val Asp
65 70 75 80
Pro Ala Pro Ala Ala Leu Asn Val Arg Glu Pro Gly Trp Leu Gly Gly
Leu Phe Asp Gly Ala Leu Leu Gln Val Leu Leu Asn Phe Leu Arg Lys
Ser Thr Asp Val Leu Met Asp Thr Arg Glu Ala Glu Ser Leu Glu Val
                               120
Glu Xaa
    130
<210> 151
<211> 62
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (62)
<223> Xaa equals stop translation
<400> 151
Met Leu Phe Trp Ala Tyr Pro Ile Cys Val Phe Ile Asp Ser Leu Ser
1 5 10 15
Cys Gln Pro Cys Leu Trp Ser Thr Gly Ala Thr Ser His Phe Asn Ser 20 25 30
```

Pro Thr Thr Ser Pro Lcu Phe Thr Leu Phe Met Pro Cys Ala Leu Ala 35 40 45

Pro Asn Pro Phe Thr Gln Leu Gly Lys Leu Asp Asp Arg Xaa 50 55 60

<210> 152

<211> 225

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (225)

<223> Xaa equals stop translation

<400> 152

Met Gly Ile Phe Pro Gly Ile Ile Leu Ile Phe Leu Arg Val Lys Phe 1 5 10 15

Ala Thr Ala Ala Val Ile Val Ser Gly His Gln Lys Ser Thr Thr Val  $20 \\ 25 \\ 30$ 

Ser His Glu Met Ser Gly Leu Asn Trp Lys Pro Phc Val Tyr Gly Gly 35 40 45

Leu Ala Ser Ile Val Ala Glu Phe Gly Thr Fhe Pro Val Asp Leu Thr 50 55 60

Lys Thr Arg Leu Gln Val Gln Gly Gln Ser Ile Asp ala Arg Phe Lys 65 70 75 80

Glu Ile Lys Tyr Arg Gly Met Phe His Ala Leu Phe Arg Ile Cys Lys 85 90 . 95

Glu Glu Gly Val Leu Ala Leu Tyr Ser Gly Ile Ala Pro Ala Leu Leu 100 105 110

Arg Gln Ala Ser Tyr Gly Thr Ile Lys Ile Gly Ile Tyr Cln Ser Leu 115 120 125

Lys Arg Leu Phe Val Glu Arg Leu Glu Asp Glu Thr Leu Leu Ile Asn 130 135 140

Met Ile Cys Gly Val Val Ser Gly Val Ile Ser Ser Thr Ile Ala Asn 145 150 155 160

Pro Thr Asp Val Leu Lys Ile Arg Met Gln Ala Gln Gly Ser Leu Phe 165 170 175

Gln Gly Ser Met Ile Gly Ser Phe Ile Asp Ile Tyr Gln Glu Gly 180 185 190 190

Thr Arg Gly Leu Trp Arg Val Ser Thr Leu Phe Leu Leu Ser Tyr 195 200 205

Thr Leu Ser Ser Tyr Asn Leu Gln Arg Ile Phe Phe Tyr Ile Lys Thr 210 215 220

Ser Tyr Val Xaa

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Xaa
 225
 <210> 153
<211> 69
<212> PRT
 <213> Homo sapiens
 <220>
 <221> SITE
 <222> (69)
 <223> Xaa equals stop translation
 <400> 153
Met Leu Met Leu Leu Thr Leu Leu Val Leu Gly Met Val Trp Val Ala
1 5 10 15
Ser Ala Ile Val Asp Lys Asn Lys Ala Asn Arg Glu Ser Leu Tyr Asp
20 25 30
Phe Trp Glu Tyr Tyr Leu Pro Tyr Leu Tyr Ser Cys Ile Ser Phe Leu 35 40 45
Gly Val Leu Leu Leu Ala Ala Gly Arg Pro Gly Gly Ala Ala Val50 \\ 55 \\ 60
Leu Leu Ser Leu Xaa
65
 <210> 154
 <211> 84
 <212> PRT
<213> Homo sapiens
<220>
<221> SITE <222> (84)
<223> Xaa equals stop translation
<400> 154
Met Tyr Gly Val Cys Leu Cys Val Ile Val Cys Val Ser Gly Val Ser
1 5 10 15
Leu Cys Leu Tyr Val Trp Gly Val Ser Val Cys Asp Cys Val Ser Val 20 25 30
Phe Met Cys Val Cys Leu Cys Val Ile Phe Cys Val Tyr Gly Lys Pro 35 \hspace{1cm} 40 \hspace{1cm} 45
Arg Thr Glu His Tyr His Ser Pro His Leu Ala Lys Gln Lys Ala Phe 50 55 60
Arg Glu Met Cys Gly Arg His Asp Val Ser Ala Ala Gly Ile Phe Gln 65 70 75 80
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<210> 155
 <211> 61
 <212> PRT
 <213> Homo sapiens
<220>
<221> SITE
<222> (61)
<223> Xaa equals stop translation
<400> 155
Met His Val Leu Leu Phe Ser Phe Leu Ile Pro Phe Leu Leu Leu Ser 1 5 10 15
Pro Val Gly Val Thr Cys Asn Ser His Met Leu Glu Arg Gln Val Ser 20 25 30
Trp Leu Lys Lys Arg Ser Thr Gln Ala Ser Gln Gln Phe Asn Lys Phe 35 40 45
Leu Arg Gly Ile Ser Asn Val Gly Arg Ile Val Ile Xaa 50 55 60
<210> 156
<211> 84
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (84)
<223> Xaa equals stop translation
<400> 156
Met Cys Leu Leu Val Glu Tyr Ser Leu Met Ile Leu Thr Ile Ile Pro
Ser Leu Leu Ser Phe Val Leu Cys Leu Lys Gly Ile Lys His Gly Asn 20 25 30
Tyr Ile Phe Gln Thr Pro Leu Pro Glu Gly Tyr Gly Trp Ile Ser Ala 35 40 45
Mct Ser Gly Leu Cys Ile Lys Phe Gly Arg Arg Lys Arg Lys Thr 50 55 60
Trp Leu Leu Gln Val Gly Thr Leu Ala Thr Ile Asp Thr Glu Phe Ala
65 70 75 80
```

<210> 157 <211> 162

Arg Ser Cys Xaa

```
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (162)
<223> Xaa equals stop translation
<400> 157
Met Ala Leu Ser Leu Thr Leu Cys Phe Val Met Phe Trp Thr Pro Asn
Val Ser Glu Lys Ile Leu Ile Asp Ile Ile Gly Val Asp Phe Ala Phe 20 25 . 30
Ala Glu Leu Cys Val Val Pro Leu Arg Ile Phe Ser Phe Pro Val 35 40 45
Pro Val Thr Val Arg Ala His Leu Thr Gly Trp Leu Met Thr Leu Lys 50 \hspace{1cm} 55
Lys Thr Phe Val Leu Ala Pro Ser Ser Val Leu Arg Ile Ile Val Leu
65 70 75 80
Ile Ala Ser Leu Val Val Leu Pro Tyr Leu Gly Val His Gly Ala Thr
Leu Gly Val Gly Ser Leu Leu Ala Gly Phe Val Gly Glu Ser Thr Met 100 105 110
Val Ala Ile Ala Ala Cys Tyr Val Tyr Arg Lys Gln Lys Lys Met
115 120 125
Glu Asn Glu Ser Ala Thr Glu Gly Glu Asp Ser Ala Met Thr Asp Net
Pro Pro Thr Glu Glu Val Thr Asp Ile Val Glu Met Arg Glu Glu Asn
145
Glu Xaa
<210> 158
<211> 146
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (107)
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<223> Xaa equals any of the naturally occurring L-amino acids

<220>

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<221> SITE
<222> (111)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (122)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (132)
<223> Xaa equals any of the naturally occurring L-amino acids
Met Glu Pro Gln Leu Gly Pro Glu Ala Ala Ala Leu Arg Pro Gly Trp

1 5 10 15
Leu Ala Leu Leu Eur Trp Val Ser Ala Leu Ser Cys Ser Phe Ser Leu 20 25 30
Pro Ala Ser Ser Leu Ser Ser Leu Val Pro Gln Val Arg Thr Ser Tyr 35 40 45
Asn Phe Gly Arg Thr Phe Leu Gly Leu Asp Lys Cys Asn Ala Cys Ile 50 55 60 .
Gly Thr Ser Ile Cys Lys Lys Phe Phe Lys Glu Glu Ile Arg Ser Asp 65 70 75 80
Asn Trp Leu Ala Ser His Leu Gly Thr Ala Ser Arg Phe Pro Leu Xaa
85 90 95
Ser Tyr Pro Cys Lys Leu Leu Gln Met Ile Xaa Lys Ile Trp Xaa Pro
                                  105
Cys Gly Xaa Leu Leu Thr Gly Gln Gln Xaa Ser Asn Glu Ile Ser Lys
                              120
Gln Glu Ile Xaa Cys Leu Leu His Pro Pro Pro Lys Asn Leu His Ile
130 135 140
Asp Val
145
<210> 159
<211> 143
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (143)
```

<223> Xaa equals stop translation

<400> 159

Met Trp Trp Ala Val Met Gly Gly Val Ile Gly Ser Trp Leu Ser Pro 1 5 10 15

Leu Ser Ile Ala Glu Cys Cys His Asp Leu Trp Thr Ser Gln Ser Cys 20 . 25 30

Glu His Ala Gly Ala Leu Cys Gly Asp Leu Leu Cys Ala Cys Arg Lys  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Val Gly Val Trp Cys Ala Leu Gln Gln His Trp Trp Asn Arg Cys Val 50 55 60

Cys Pro His Ala Val Ile Arg Val His Cys Thr Gly Ala Ser Tyr Thr 65 70 75 80

Leu Gln Lys Ile Cys Ser Cys Asn Pro Lys Phe Met Gly Arg His Pro 85 90 95

His Arg Trp Gln Gln Ile Arg Lys Cys Ser Gln Pro Val Leu Arg Gly 100 105 110

Ser Arg Ala Ala Phe Ile Trp Val Arg Leu Ala Ala Leu Asn Phe Ile 115 120 125

Ser Ser Phe Arg Cys Ile Ser Leu Ile Ser Tyr Ser Ala Phe Xaa 130 135 140

<210> 160

<211> 51

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (51)

<223> Xaa equals stop translation

<400> 160

Met Lys Val Ser Asp Phe Asn Phe Leu Ile Phe Leu Ile Phe Ala Leu

1 5 10 15

Phe Leu Thr Leu Glu Ala Phc Leu Lys Phe Thr Lys Arg Val Leu Ala 20 25 30

Val Val Gly Asn Leu Pro Glu Pro Pro Ile Ile Lys Thr Ile Gly Phe 35 40 45

Leu Tyr Xaa 50

<210> 161

<210> 161 <211> 65

<211> 05 <212> PRT

<213> Homo sapiens

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<220>
<221> SITE
 <222> (65)
<223> Xaa equals stop translation
Met Val Trp Ser Ala Ala Pro Ala Pro Cys Cys Leu Leu Gly Val Leu
1 5 10 15
Gly Leu Val Gln Val Leu Gly Ala Gln Ala Val Gly Pro Trp Thr Ala 20 25 30
Ser Ala Cys Leu Gly Ala Ala Gln Ala Gln Pro Cys Arg Pro Cys Lys
. 35 40 45
Glu Ser Ser Leu Arg Leur Phe Ser Ala Ser Ala Pro Ser Not Thr His
50 55 60
Xaa
 65
<210> 162
<211> 59
<212> PRT
<213> Homo sapiens
<220>
<221> SITE <222> (59)
<223> Xaa equals stop translation
<400> 162
Met Glu Lys Tyr Cys Leu Gly Asn Asn Met Leu Ser Arg Phe Cys Leu
1 5 10 15
Gln Arg His Thr Val Val Ser Leu Ser Lys His His Pro Phe Val Pro 35 .40 .45
Thr Asn Gly Ser Lys Ser Tyr Ser Ser Phe Xaa 50 55
<210> 163
<211> 374
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (84)
<223> Kaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
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<222> (112)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 163

Met Arg Pro Gly Thr Ala Leu Gln Ala Val Leu Leu Ala Val Leu Leu 1 5 10 15

Val Gly Leu Arg Ala Ala Thr Gly Arg Leu Leu Ser Gly Gln Pro Val 20 25 30

Cys Arg Gly Gly Thr Gln Arg Pro Cys Tyr Lys Val Ile Tyr Phe His  $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$ 

Asp Thr Ser Arg Arg Leu Asn Phe Glu Glu Ala Lys Glu Ala Cys Arg 50 55 60

Arg Asp Gly Gly Gln LeusVal Ser Ile Glu Ser Glu Asp Glu Gln Lys 65 70 75 80

Leu Ile Glu Xaa Phe Ile Glu Asn Leu Leu Pro Ser Asp Gly Asp Phe 85 90 95

Trp Ile Gly Leu Arg Arg Arg Glu Glu Lys Gln Ser Asn Ser Thr Xaa 100 105 110

Cys Gln Asp Leu Tyr Ala Trp Thr Asp Gly Ser Ile Ser Gln Phe Arg 115 120 125

Asn Trp Tyr Val Asp Glu Pro Ser Cys Gly Ser Glu Val Cys Val Val 130 135 140

Met Tyr His Gln Pro Ser Ala Pro Ala Gly Ile Gly Gly Pro Tyr Met 145 150 155 160

Phe Gln Trp Asn Asp Asp Arg Cys Asr Met Lys Asn Asn Phe Ile Cys 165 170 175

Lys Tyr Ser Asp Glu Lys Pro Ala Val Pro Ser Arg Giu Ala Glu Gly 180 185 190

Glu Glu Thr Glu Leu Thr Thr Pro Val Leu Pro Glu Glu Thr Gln Glu 195 200 205

Glu Asp Ala Lys Lys Thr Phe Lys Glu Ser Arg Glu Ala Ala Leu Asn 210 215 220

Leu Ala Tyr Ile Leu Ile Pro Ser Ile Pro Leu Leu Leu Leu Val 225 230 235 240

Val Thr Thr Val Val Cys Trp Val Trp Ile Cys Arg Lys Arg Lys Arg 245 250 255

Glu Gln Pro Asp Pro Ser Thr Lys Lys Gln His Thr Ile Trp Pro Ser 260 265 270

Pro His Gln Gly Asn Ser Pro Asp Leu Glu Val Tyr Asn Val Ile Arg 275 280 285

Lys Gln Ser Glu Ala Asp Leu Ala Glu Thr Arg Pro Asp Lou Lys Asn

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290 295 300 Ile Ser Phe Arg Val Cys Ser Gly Glu Ala Thr Pro Asp Asp Met Ser 305  $\phantom{\bigg|}310\phantom{\bigg|}315\phantom{\bigg|}315\phantom{\bigg|}$ Cys Asp Tyr Asp Asn Met Ala Val Asn Pro Ser Glu Ser Gly Phc Val 325 330 335 Phe Ser Pro Asp Gln Met Gly Arg Ser Lys Glu Ser Gly Trp Val Glu 355 360 365 Asn Glu Ile Tyr Gly Tyr <210> 164 <211> 64 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (64) <223> Xaa equals stop translation <400> 164 Met His Pro Gln Leu Ile Pro Ser Val Ile Ala Val Val Phe Ile Leu 1 5 10 15 Leu Leu Gly Val Cys Phe Ile Ala Ser Cys Leu Val Thr His His Asn  $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$ Phe Ser Arg Cys Lys Arg Gly Thr Gly Val His Lys Leu Glu His His  $35 \hspace{1cm} 40 \hspace{1cm} 45$ Ala Lys Leu Lys Cys Ile Lys Glu Lys Ser Glu Leu Lys Ser Cys Xaa 50 60<210> 165

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<210> 165
<211> 743
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (743)
<223> Xaa equals stop translation

<400> 165
Het Ala Val Arg Glu Leu Cys Phe Pro Arg Gln Arg Gln Val Leu Phe
1 5 10 15
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Leu Phe Leu Phe Trp Gly Val Ser Leu Ala Gly Ser Gly Phe Gly Arg 20 25 30Tyr Ser Val Thr Glu Glu Thr Glu Lys Gly Ser Phe Val Val Asn Leu 35 40 45 Ala Lys Asp Leu Gly Leu Ala Glu Glu Glu Leu Ala Ala Arg Gly Thr  $50 \hspace{1cm} 55 \hspace{1cm} 60$ Arg Val Val Ser Asp Asp Asn Lys Gln Tyr Leu Leu Leu Asp Ser His 65 70 75 80 Thr Gly Asn Leu Leu Thr Asn Glu Lys Leu Asp Arg Glu Lys Leu Cys
85 .90 .95 Gly Pro Lys Glu Pro Cys Net Leu Tyr Phe Gln Ile Leu Met Asp Asp 100 105 110 Pro Phe Glu Ile Tyr Arg Ala Glu Leu Arg Val Arg Asp Ile Asn Asp 115 120 125 His Ala Pro Val Pne Glm Asp Lys Clu Thr Val Leu Lys Ile Ser Glu 130 135 140 Asn Thr Ala Glu Gly Thr Ala Phe Arg Leu Glu Arg Ala Gln Asp Pro 145 155 160 Asp Gly Gly Leu Asn Gly Ile Gln Asn Tyr Thr Ile Ser Pro Asn Ser 165 170 175 Phe Phe His Ile Asn Ile Ser Gly Gly Asp Glu Gly Met Ile Tyr Pro 180 185 190 Glu Leu Val Leu Asp Lys Ala Leu Asp Arg Glu Glu Gln Gly Glu Leu 195 200 205 Ser Leu Thr Leu Thr Ala Leu Asp Gly Gly Ser Pro Ser Arg Ser Gly 210 215 220 Thr Ser Thr Val Arg Ile Val Val Leu Asp Val Asn Asp Asn Ala Pro 225 230 235 240 Gln Phe Ala Gln Ala Leu Tyr Glu Thr Gln Ala Pro Glu Asn Ser Pro 245 250 255 Ile Gly Phe Leu Ile Val Lys Val Trp Ala Glu Asp Val Asp Ser Gly 260 265 270 Val Asn Ala Glu Val Ser Tyr Ser Phe Phe Asp Ala Ser Glu Asn Ile 275 280 285 Arg Thr Thr Phe Cln Ile Asn Pro Phe Ser Gly Glu Ile Phe Leu Arg 290 295 300 Glu Leu Leu Asp Tyr Glu Leu Val Asn Ser Tyr Lys Ile Asn Ile Gln 305 310 315 320 Ala Met Asp Gly Gly Gly Leu Ser Ala Arg Cys Arg Val Leu Val Glu 325 330 335

- Val Leu Asp Thr Asn Asp Asn Pro Pro Glu Leu Ile Val Ser Ser Phe 340 345 350
- Ser Asn Ser Val Ala Glu Asn Ser Pro Glu Thr Pro Leu Ala Val Phe 355 360 365
- Lys Ile Asn Asp Arg Asp Ser Gly Glu Asn Gly Lys Met Val Cys lyr 370 380
- Ile Gln Glu Asn Leu Pro Phe Leu Leu Lys Pro Ser Val Glu Asn Phe 385 390 395 400
- Tyr Ile Leu Ile Thr Glu Gly Ala Leu Asp Arg Glu Ile Arg Ala Glu 405 410 415
- Tyr Asn Ile Thr Ile Thr Val Thr Asp Leu Gly Thr Pro Arg Leu Lys
  420 425 430
- Thr Glu His Asn Ile Thr Val Leu Val Ser Asp Val Asn Asn Asn Ala 435 440 445
- Pro Ala Phe Thr Gln Thr Ser Tyr Thr Leu Phe Val Arg Glu Asn Asn 450 455 460
- Ser Pro Ala Leu His Ile Gly Ser Val Ser Ala Thr Asp Arg Asp Ser 465 470 475 483
- Gly Thr Asn Ala Gln Val Thr Tyr Ser Leu Leu Pro Pro Gln Asp Pro 485 490 495
- His Leu Pro Leu Ala Ser Leu Val Ser Ile Asn Ala Asp Asn Gly His 500 505 510
- Leu Phe Ala Leu Arg Ser Leu Asp Tyr Glu Ala Leu Gln Ala Phe Glu 515 520 525
- Phe Arg Val Gly Ala Thr. Asp Arg Gly Ser Pro Ala Leu Asn Ser Glu 530 535 540
- Ala Leu Gly Ala Arg Ala Gly Ala Gly Arg Gln Arg Gln Leu Ala Leu 545 550 555 560
- Arg Ala Val Pro Ala Ala Giu Arg Leu Arg Ala Leu His Arg Ala Gly 565 570 575
- Ala Pro Gly Gly Arg Ala Gly Leu Pro Gly Asp Gln Gly Gly Gly Gly 580 585 590
- Gly Arg Arg Leu Gly Pro Glu Arg Leu Ala Val Val Pro Ala Ala Gln
  595 600 605
- Gly His Gly Ala Arg Ala Val Arg Cys Val Gly Ala Glr Trp Gly Gly 610 620
- Ala His Arg Gln Ala Ala Glu Arg Ala Arg Ser Gln Ala Gln Ala 625 630 635 640
- Gly Gly Ala Cys Gln Gly Gln Trp Arg Ala Ser Ser Leu Gly His Arg

645 His Ala Ala Arg Ala Pro Gly Gly Arg Leu Leu Pro Ala Leu Pro Ala 660 665 670 Ser Pro Gly Gly Gly Pro Gly Pro Gly Pro Gly Arg Leu Ala His Arg 675 680 685 Leu Pro Gly Cly Gly Val Gly Leu Gly Val Phe Ala Leu Pro Pro Leu 690 . 695 700 Gly Ala Pro Val Arg Gly Gly Ala Ala Val Gln Glu Glu Gln Gly Gly 705 710 715 720 Leu Gly Gly Ser Leu Leu Gly Ala Arg Gly Ser Phe Ser Arg Ala Ser 725 730 735Gly Gly Arg Clu Gly Arg Xaa 740 <210> 166 <211> 214 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (214) <223> Xaa equals stop translation Met Asn Arg Met Glu Leu Leu Lys Leu Leu Leu Thr Cys Phe Ser Glu  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ Ala Met Tyr Leu Pro Pro Ala Pro Glu Ser Gly Ser Thr Asn Pro Trp 20 25 30Val Gin Phe Phe Cys Ser Thr Glu Asn Arg His Ala Leu Pro Leu Phe  $35 \hspace{1cm} 40 \hspace{1cm} 45$ Thr Ser Leu Leu Asn Thr Val Cys Ala Tyr Asp Pro Val Gly Tyr Gly 50 60Ile Pro Tyr Asn His Leu Leu Phe Ser Asp Tyr Arg Glu Pro Leu Val 65 70 75 80 Glu/Glu Ala Ala Gln Val Lcu Ile Val Thr Leu Asp His Asp Ser Ala 85 90 95 Ser Ser Ala Ser Pro Thr Val Asp Gly Thr Thr Thr Gly Thr Ala Met 100 105 110 Asp Asp Ala Asp Pro Pro Gly Pro Glu Asn Leu Phe Val Asn Tyr Leu 115 120 125

Ser Arg Ile His Arg Glu Glu Asp Phe Gln Phe Ile Leu Lys Gly Ile 130 135 140

Ala Arg Leu Leu Ser Asn Pro Leu Clu Cln Thr Tyr Leu Pro Asn Ser 145 150 155 160 Thr Lys Lys Asp Pro Val Pro Pro Gly Ala Ala Ser Ser Leu Leu Glu 165 170 175 Ala Leu Arg Leu Gln Gln Glu Ile Pro Leu Leu Arg Ala Glu Gln 180 195 190 Arg Arg Pro Arg His Pro Cys Pro His Pro Leu Leu Pro Gln Arg Cys 195 200 205 Pro Gly Arg Ser Val Xaa 210 <210> 167 <211> 213 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (213) <223> Xaa equals stop translation <400> 167 Met Pro Ser Leu Arg Phe Leu Ala Leu Ala Leu Leu Leu Ala Ile Leu 1 5 10 15 Pro Ala Leu Pro Asn Ala His Ala Ala Pro Gly Ile Gly Leu Ile 20 25 30 Gly Gly Ser Gln Ala Ser Ala Lys Glu Glu Pro Gln Ser Asn Ala  $35 \hspace{1cm} 40 \hspace{1cm} 45$ Gln Pro Ser Ala Asp Glu Arg Lys Gln Arg Leu Leu Ser Gln Ala Glu 50 55 60 Glu Thr Arg Gln Arg Leu Thr Asp Leu Lys Ala Glu Leu Ala Gly Ala 65 70 75 80 Pro Lys Glu Ile Ser Glu Ala Gln Arg Thr Leu Ser Lys Leu Val Ser 85 90 95 Glu Asp Asn Ser Asp Leu Pro Glu Arg Leu Ser Lys Leu Ser Val Pro 100 105 110 Val Leu Glu Gln Arg Leu Ala Ala Arg Val Asp Glu Leu Ala Leu Trp 115 120 125 Gln Gln Ala Leu Ser Ala Ala Asn Ser Met Leu Ile Ser Ala Gln Thr 130 135 140 Arg Pro Glu Arg Ala Gln Ala Asp Ile Ser Lys Asn Gln Leu Árg Ile 145 150 155 160

Asp Glu Ile Asn Gly Leu Leu Lys Ser Gly Arg Glu Asn Asn Lys Pro 165 170 175

```
Leu Thr Asp Glu Arg Arg Ala Leu Leu Glu Ser Thr Ser Arg Ala Ala
            180
                                185
```

Ala Gly Pro Ser Ile Phe His Pro Gly Gly Val Pro Gly Lys Cys Thr 200

Gln Phe Ala Leu Xaa 210

<210> 168

<211> 75

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (75)

<223> Xaa equals stop translation

Met Phe Thr Scr Phe Gly Leu Ala Ser Pro Arg Ile Leu Phe Cys Phe 1 5 10 15

Cys Phe Phe Asp Leu Gly Phe Ile Phe Phe Cys Val Leu Tyr Tyr Ile  $20 \hspace{1cm} 25 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}$ 

Val Lys Gly Ile Leu Ala Glu Thr Leu Val Phe Gly Ala Arg Gly Glu 35 40 45

Gln Glu Cys Trp Ala Val Tyr Phe Arg Trp Arg Thr His Leu Gln Thr 50 60

Phe Gly Leu Phe Ser Phe Asn Cys Ser Val Xaa

<210> 169 <211> 48

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (48)

<223> Xaa equals stop translation

<400> 169

Met Phe Leu Cys Leu Phe Phe Phe Phe Phe Asn Ala Thr Gln Gly Asn

Ile Phe Ile Ser Phe Leu Ser Gly Leu Pro Gln Cys Ile Phe Ile Ser

Phe Glu Thr Lys Arg Phe Trp Lys Leu Phe Phe Cys Ser Phe Lys Xaa 15 40 45

<213> Homo sapiens

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<210> 170
 <211> 88
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SITE
 <222> (88)
 <223> Xaa equals stop translation
 <400> 170
<400> 170
Met Gly Leu His Leu Arg Pro Tyr Arg Val Gly Leu Leu Pro Asp Gly
10
15
Leu Leu Phe Leu Leu Leu Leu Met Leu Leu Ala Asp Pro Ala Leu 20 25 30
Pro Ala Gly Arg His Pro Pro Val Val Leu Val Pro Gly Asp Leu Gly 35 40 45
Asn Gln Leu Glu Ala Lys Leu Asp Lys Pro Thr Val Val His Tyr Leu 50 \hspace{1cm} 55 \hspace{1cm} 60 \hspace{1cm}
Cys Ser Lys Lys Thr Glu Scr Tyr the Thr Ile Trp Leu Asn Leu Glu 65 70 75 80
Leu Leu Pro Val His His Xaa
<210> 171
<211> 42
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation
<400> 171
Met Ala Cys Glu Thr His Gly Val Leu Val Pro Ala His Leu Ser Gly
Leu Ile Thr Cys Leu Leu Ala Phe Trp Val Pro Ala Ser Cys 1le Gln 20 25 30
Arg Cys Ser Gly Ser Pro Leu Pro Leu Xaa
         35
<210> 172
<211> 48
<212> PRT
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<220>

<221> SITE

<222> (48)

<223> Xaa equals stop translation

<400> 172

Met Gln Cys Phe Leu Phe Ser Ile Phe Leu Ile Thr Gly Leu Ala Glu
1 5 10 15

Glu Phe Cys Glu Gln Leu Ser Ile Ser Leu Ala Glu Glu Glu Ile Gln

Leu Ser Ser Thr Val Glu His Phe Cys Met Thr Ala Phe Ser Trp Xaa 40

<210> 173

<211> 233 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (233)

<223> Kaa equals stop translation

<400> 173

Met Ala Ala Leu Ala Ala Ala Ala Lys Lys Val Trp Ser Ala Arg Arg
1 5 10 15

Leu Leu Val Leu Leu Phe Thr Pro Leu Ala Leu Leu Pro Val Val Phe 20 25 30

Ala Leu Pro Pro Lys Glu Gly Arg Cys Leu Phe Val Ile Leu Leu Met 35 40 45

Ala Val Tyr Trp Cys Thr Glu Ala Leu Pro Leu Ser Val Thr Ala Leu 50 60

Leu Pro Ile Val Leu Phe Pro Phe Met Gly Ile Leu Pro Ser Asn Lys

Val Cys Pro Gln Tyr Phe Leu Asp Thr Asn Phe Leu Phe Leu Ser Cly

Leu Ile Met Ala Ser Ala Ile Glu Glu Trp Asn Leu His Arg Arg Ile 100 105 110

Ala Leu Lys Ile Leu Met Leu Val Gly Val Gln Pro Ala Arg Leu Ile 115 120 125

Leu Gly Met Net Val Thr Thr Ser Phe Leu Ser Met Trp Leu Ser Asn

Thr Ala Ser Thr Ala Met Met Leu Pro Ile Ala Asn Ala Ile Leu Lys 145 150 155 160

```
Ser Leu Phe Gly 3ln Lys Glu Val Arg Lys Asp Pro Ser Cln Glu Ser
165 170 175
 Glu Glu Asn Thr Gly Ile Glu Pro Asn Thr Phe Leu Ser Glu Glu Arg
              180
                                    185
 Leu Lys Leu Gln Ala Pro Leu Val Ile Arg Leu Gly Gln Ile Thr Glu
Ser Gly Gln Trp Asn Met Ser Gly Asn Asp Val Cys Asn Phe Arg Val
210 215 220
Leu Ser Phe Leu Pro Gly Gly Met Xaa .
                       230
<210> 174
<211> 45
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (45)
<223> Kaa equals stop translation
<400> 174
Met Gly Thr Ile Phe Gly Tyr Leu His Cys Val Lys Cys Tyr Val Leu
1 5 10 15
                                                              15
Tyr Phe Ile Phe Ile Leu Ile Thr Ala Val Tyr His Ser Phe Tyr Tyr
Pro His Tyr Arg Gly Lys Ala Leu Ile Ser Gly Thr Xaa
35 40 45
<210> 175
<211> 85
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (77)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (85)
<223> Xaa equals stop translation
<400> 175
```

Met Val Trp Phe Leu Phe Leu Val Phe Ile Phe Leu Lys Val Lys Gly

10

Ile Thr Gly Val Ser His Arg Leu Gln Pro Gln Ile Leu Phe Ser Arg 35 40 45His Lys His Asn Gin Glu Ile Ile Leu Gln Met Val Ser Phe Ser Cys 50 55 60 Cys Val Phe Phe Pro Met Ile Arg Glu Val Lys Ser Xaa Leu Gly Cys 65 70 75 80 Ile Lys Met Ser Xaa <210> 176 <211> 66 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (66) <223> Xaa equals stop translation <400> 176 Met Trp Val Leu Leu Ser Cys Pro Leu Pro Pro Leu Cys Leu Pro Ala 1 5 10 15 Ser Ala Val Pro Gly Gln Cys Leu Gly Gly Gln Trp Ser Gly His Gln 20 25 30Leu Arg Leu Arg Gly Arg Gly Trp His Cys Arg Cys His Cys Arg Ala 35 40 45 Trp Ala Ala Asp Met Gly Arg Gly Leu His Ser Cys Gln Leu Leu Ser Arg Xaa 65 <210> 177 <211> 55 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (55) <223> Xaa equals stop translation <400> 177 Met Leu Leu Cys Ile Leu Leu Ile Phe Cys Val Val Gly Leu Ser 1 5 10 Val Val Gly Arg Arg Val Leu Lys Ser Thr Thr Ile Ile Val Tyr Leu Ser Ile Thr Pro Phe Ser Ser Phe Ser Ser Ile Ser His Ile Phe Gln

<400> 179

1

```
35
                               40
                                                   45
Leu Leu Ile Gly Ala His Xaa
<210> 178
<211> 83
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (4)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (83)
<223> Xaa equals stop translation
<400> 178
Met Cys Val Xaa Leu Ser Phe Cys Pro Phe Leu Ser Ser Ala Leu Pro
Ala Ser His Thr Gln Phe Tyr Met Pro Arg Gly Ala Lys Phe Gly Thr
Phe Thr Leu Gln Ala Ser Val Ser Pro Leu Glu Glu Lys Thr His Ser
Phe Thr His Pro Gly Ile Gly Cly Lys Leu Leu Gly His Gln Asp Pro
Gly Ala Pro Gly Pro Ser Trp Asn Ile Arg Ser Thr Trp Ser Thr Arg 65 70 75 80
Ser Leu Xaa
<210> 179
<211> 330
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (247)
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<223> Xaa equals any of the naturally occurring L-amino acids

Met Ser Pro Leu Ser Ala Ala Arg Ala Ala Leu Arg Val Tyr Ala Val

Gly Ala Ala Val Ile Leu Ala Gln Leu Leu Arg Arg Cys Arg Gly Gly 20 25 30

Phe Leu Glu Pro Val Xaa Pro Pro Arg Pro Asp Arg Val Ala Ile Val 35 45

Thr Gly Gly Thr Asp Gly Ile Gly Tyr Ser Thr Ala Lys His Leu Ala 50 60

Arg Leu Gly Met His Val Ile Ile Ala Gly Asn Asn Asp Ser Lys Ala 65 70 75 80

Lys Gln Val Val Ser Lys Ile Lys Glu Glu Thr Leu Asn Asp Lys Val 85 90 95

Glu Phe Leu Tyr Cys Asp Leu Ala Ser Met Thr Ser Ile Arg Gln Phe 100 105 110

Val Gln Lys Phe Lys Met Lys Lys Ile Pro Leu His Val Leu Ile Asn .115 120 125

Asn Ala Gly Val Met Met Val Pro Gln Arg Lys Thr Arg Asp Gly Phe 130 135 140

Glu Glu His Phe Gly Leu Asn Tyr Leu Gly His Phe Leu Leu Thr Asn 145 150 155 160

Leu Leu Leu Asp Thr Leu Lys Glu Ser Gly Ser Pro Gly His Ser Ala 165 170 175

Arg Val Val Thr Val Ser Ser Ala Thr His Tyr Val Ala Glu Leu Asn 180 185 190

Met Asp Asp Leu Gln Ser Ser Ala Cys Tyr Ser Pro His Ala Ala Tyr 195 200 205

Ala Gln Ser Lys Leu Aia Leu Val Leu Phe Thr Tyr His Leu Gln Arg 210 215 220

Leu Leu Ala Ala Glu Gly Ser His Val Thr Ala Asn Val Val Asp Pro 225 230 240

Leu Ala Lys Lys Leu Leu Gly Trp Leu Leu Phe Lys Thr Pro Asp Glu 260 265 270

Gly Ala Trp Thr Ser Ile Tyr Ala Ala Val Thr Pro Glu Leu Glu Gly 275 280 285

Val Gly Gly Arg Tyr Leu Tyr Asn Glu Lys Glu Thr Lys Ser Leu His 290 295 300

Val Thr Tyr Asn Gln Lys Lcu Gln Gln Gln Leu Trp Ser Lys Ser Cys 305 310 315 320

Glu Met Thr Gly Val Leu Asp Val Thr Leu

325

<223> Xaa equals stop translation

<400> 182

330

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<210> 180
<211> 41
<212> PRT
 <213> Homo sapiens
 <220>
 <221> SITE
 <222> (41)
<223> Xaa equals stop translation
 <400> 180
Met lie Ala Cys Gin Tyr Ile Ser Leu Ala Ile Met Leu Ala Phe Val
1 5 10 15
Arg Trp Ala Ala Phe Leu Leu Phe Pro Phe Leu Cys Gly Asp Asn Gly 20 25 30
Gly Asn Ile Gln Gln Lys Tyr Val Xaa
          35
<210> 181
<211> 52
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (52)
<223> Xaa equals stop translation
<400> 181
Met Ala Asn Ala Met Ala Tyr Leu Ser Ile Phe Leu Cys Gly Ala Ser
1 5 10 15
Ser Ser Pro Cys Asp Cys Ala Leu Leu Val Pro Val Scr Leu Phe Arg 20 25 30
Gly Arg Lys Val Ala Asn Phe Lys Asn Gln Asn Ser Asp Val Thr Ser 35 40 45
Gly Asn Ala Xaa
     50
<210> 182
<211> 55
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (55)
```

```
Met Gln Gln Ile Cys Ser Cys Leu Gly Ala Phe Ala Leu Leu Phe Phe 1 5 10 15 \cdot
```

Trp Pro Gly His Phe Thr Ser Thr Phe Ser Ile Phe Tyr Asp Phe Leu 20 25 30

Pro Ile Phe Gly Ser Leu Phe Lys Cys His Pro Ser Lys Arg Pro Ser 35 40 45

Lys Leu Pro Tyr Leu Lys Xaa 50 55

<210> 183

<211> 62

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (62)

<223> Xaa equals stop translation

<400> 183

Met Arg Leu Leu Leu Glu Trp Arg Val Tyr Leu Arg Leu Thr Cys Ala 1 5 10 15

Thr Lys Asp Gly Met Ala Arg Glu Cys Pro Thr Thr Trp Leu Ser Pro 20 25 30

Pro Ala Lys Pro Asp Phe Ala Gln Arg His Ser Val Lys Pro Thr Ala  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Leu Gln Gly Gly Arg Trp Ser Arg Leu Gly Ala Ser Pro Xaa 50 55 60

<210> 184

<211> 148

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (148)

<223> Xaa equals stop translation

<400> 184

Met Leu Gly Leu Pro Trp Lys Gly Gly Leu Ser Trp Ala Leu Leu Leu 1 5 10 15

Leu Leu Gly Ser Gln Ile Leu Leu Iie Tyr Ala Trp His Phe His 20 25 30

Glu Gln Arg Asp Cys Asp Glu His Asn Val Met Ala Arg Tyr Leu Pro  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Ala Thr Val Glu Phe Ala Val His Thr Phe Asn Gln Gln Ser Lys Asp 50 55 60

```
Tyr Tyr Ala Tyr Arg Leu Gly His Ile Leu Asn Ser Trp Lys Glu Gln 65 70 75 80
 Val Glu Ser Lys Thr Val Phe Ser Met Glu Leu Leu Gly Arg Thr
 Arg Cys Gly Lys Phe Glu Asp Asp Ile Asp Asn Cys His Phe Gln Glu 100 105 110
 Ser Thr Clu Leu Asn Asn Thr Phe Thr Cys Phe Phe Thr Ile Ser Thr 115 120 125
Arg Pro Trp Met Thr Gln Phe Ser Leu Leu Asn Lys Thr Cys Leu Glu
130 135 140
Gly Phe His Xaa
 <210> 185
 <211> 161
 <212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (146)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (151)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (161)
<223> Xaa equals stop translation
<400> 185
Met Arg Leu Leu Cys Gly Leu Trp Leu Trp Leu Ser Leu Leu Lys Val
1 5 10 15
Leu Gln Ala Gln Thr Pro Thr Pro Leu Pro Leu Pro Pro Pro Met Gln 20 25 30
Ser Phe Gln Gly Asn Gln Phe Gln Gly Glu Trp Phe Val Leu Gly Leu 35 40 45
Ala Gly Asn Ser Phe Arg Pro Glu His Arg Ala Leu Leu Asn Ala Phe
50 55 60
Thr Ala Thr Phe Glu Leu Ser Asp Asp Gly Arg Phe Glu Val Trp Asn 65 70 75 80
Ala Met Thr Arg Gly Gln His Cys Asp Thr Trp Ser Tyr Val Leu Ile
85 90 95
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Pro Ala Ala Gln Pro Gly Gln Phe Thr Val Asp His Gly Val Gly Arg 105

Ser Trp Leu Leu Pro Pro Gly Thr Leu Asp Gln Phe Ile Cys Leu Gly 115 120 120 125

Arg Ala Gln Giy Leu Ser Asp Asp Asn Ile Val Phe Pro Asp Val Thr 130 135 140

Gly Kaa Ala Leu Asp Leu Kaa Ser Leu Pro Trp Val Ala Ala Pro Ala 145  $\phantom{\bigg|}150\phantom{\bigg|}150\phantom{\bigg|}155\phantom{\bigg|}160\phantom{\bigg|}$ 

Xaa

<210> 186 <211> 122

<212> PRT

<213> Homo sapiens

<221> SITE

<222> (122)

<223> Xaa equals stop translation

<400> 186

Met Met Leu Pro Gln Trp Leu Leu Leu Leu Phe Leu Leu Phe Phe

Leu Phe Leu Leu Thr Arg Gly Ser Leu Ser Pro Thr Lys Tyr Asn Leu 20 25 30

Leu Glu Leu Lys Glu Ser Cys Ile Arg Asn Gln Asp Cys Glu Thr Gly  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Cys Cys Gln Arg Ala Pro Asp Asn Cys Glu Ser His Cys Ala Glu Lys 50 60

Gly Ser Glu Gly Ser Leu Cys Gln Thr Gln Val Phe Phe Gly Gln Tyr 65 70 75 80

Arg Ala Cys Pro Cys Leu Arg Asn Leu Thr Cys Ile Tyr Ser Lys Asn 85 90 95

Glu Lys Trp Leu Ser Ile Ala Tyr Gly Arg Cys Gln Lys Ile Gly Arg

Gln Lys Leu Ala Lys Lys Met Phe Phe Xaa

<210> 187

<211> 163

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (163) <223> Xaa equals stop translation

<400> 187

Met Thr Ser Asn Phe Pro Phe Cys Thr Leu Ile Leu Gly Ile Ala Gln
1 5 10 15

Ala Cln Ala Cys Pro Gly Cys Pro Gly Asp Trp Pro Gly Leu Gly Ser 20 25 30

Gly Val Gly Glu Gly Leu His His Ile Arg Thr Cys Arg Thr Pro Ile 35 40 45

Pro Cys Ser Pro Pro Ala Pro Ala Ala Ala Cys Leu Gly Ser Gly His  $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$ 

Ala Arg Leu Pro Cys Val Leu Arg Leu Trp Pro Val Pro Ala Asn Leu 65 70 75 80

Ser Ser Pro Phe Arg Leu Glu Ala Leu His Cys Ser Phe Trp Ser Ser 85  $\phantom{0}90\phantom{0}$  95

Pro Leu Leu Pro Ala Pro His Leu Ala Phe Phe Gly Phe Arg Asp Leu 100 105 110

Leu Thr Asp Phe Leu Leu Ala Ala Cys Leu Leu Thr Phe Gln Lys Thr 115 120 125

Pro Leu Glu Leu Pro Met Ala Val Val His Leu Leu Val Ala Thr Pro 130 135 140

Cys Tyr Gln Met Leu Asp Asn Leu Pro Leu Pro Ser Ala Ala Ala Asn 145 150 150 160

Trp Cys Xaa

<210> 188

<211> 51 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (51)

<223> Xaa equals stop translation

<400> 188

Met Pro Gly Ile Leu Ala Gly Ile Pro Val Lys Asp Leu Cys Leu Ser  $\frac{1}{5}$  5 10 15

Leu Leu Gln Gly Phe Arg Leu Leu Leu Leu Cys Val Cys Pro Gly Trp 20 25 30

Leu Ser Gly Trp Met Gly Gly Gln Lys Cly Ser Pro Arg Ile Val Asp 35 40 45

Ile Gly Xaa

50

<221> SITE <222> (144)

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<210> 189
<211> 65
 <212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (65)
<223> Xaa equals stop translation
<400> 189
Met Tyr Leu Tyr Leu Gly Val Phe Phe His Leu Ile Tyr Pro Gly Ala
1 5 10 15
Leu Ser Ile Thr Thr Leu Sly Lys His Ser His Pro Phe Phe Thr Ala
                                                         30
Glu Gln Asn Ser Thr Val Trp Met Glu His Thr Leu Phe His Gln Ser
          35
Pro Val Ala Ser His Leu Val Cys Phe Gln Ser Phe Ala Phe Ser Glu
                           55
Xaa
 65
<210> 190
<211> 47
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (47)
<223> Xaa equals stop translation
<400> 190
Met Thr Leu Ser Leu Cln Leu Ala Glu Leu Val His Phe Val Cys Ala
1 5 10 15
Phe Gln Ser Gln Trp Thr Gly Val Tyr Pro Met Met Pro Pro Leu Lys 20 25 30
Pro Thr Glu Pro Leu Cys Phe Ala Cys Val Pro Cys Arg Val Xaa
35 40 45
<210> 191
<211> 144
<212> PRT
<213> Homo sapiens
<220>
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<223> Xaa equals stop translation

<400> 191

Met Ser Pro Phe His Leu Leu Gly Leu Lys Val Phe Leu Thr Trp Ala 1 5 10 15

Leu Thr Leu Ala Gln Ile Cys Leu Tyr Phe Phe Glu Val Gln Pro Leu 20 25 30

Gly Leu Leu Ala Leu Asn Phe Phe Cys Thr Ala Thr Ala Gly Leu Lys

Glu Leu Cys Met His Pro Pro Ser Leu Ala Phe Thr Pro Glu Phe His  $50 \hspace{1cm} 55 \hspace{1cm} 60 \hspace{1cm}$ 

Thr Ser Leu Ser Pro Leu Ala Ile Pro Ser Phe Cys Gly Thr Ser Val 65 70 75 80

Ser Leu Ser Asn Ser His Thr Ile Pro Leu Ser Leu Tyr Leu Pro Phe 85 90 95

Pro Ser Lys Ser Arg Met Pro Asp Thr Leu His Leu Leu Val His Ser 100 105 110

Leu Pro Leu Val His Ser Gln Val Leu Pro Val Lys Asp Val Thr Ile 115 120 125

Glu Trp Pro Leu Cys Gln Arg Cys Leu Gly Ser Thr Cys His Gln Xaa 130 135 140

<210> 192

<211> 81

<212> PRT

<213> Homo sapiens

<220>

<221> SITE <222> (76)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (81)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 192

Met Phe Cys Phe Ser Ser Ile Phe Cys Ser His Glu His Thr His Leu 1 5 10 15

Pro Gly Thr Phe Trp Leu Phe Leu Phe Leu Phe Leu Phe Leu Pro Pro 20 25 30

Ser Cys Pro Cys Phe Leu Pro Phe Ser Leu Ala Ile Glu Thr Val Arg 35 40 45

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Trp Pro Cys Trp His His Pro Thr Ser Phe Glu Leu Cys Tyr Pro Gly
 Thr Ser Ile Tyr Tyr Ala Ser Arg Gly Gly Pro Xaa Pro Asn Ser Glu 65 70 75 80
 Xaa
 <210> 193
 <211> 45
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SITE <222> (45)
 <223> Xaa equals stop translation
 <400> 193
Met Thr Tyr Leu Pho Cys Ser Ser Ile Ser Leu Leu Leu Leu Lys Val
1 5 . 10 15
His Ser Ser Gly His Gln Asp Ile Arg Lys Ala Lys Ser Lys Val Pro . 20 25 30
Arg Leu Leu Ile Ile Gln Cys Pro Gln Gln Arg Glu Xaa
35 40 45
<210> 194
<211> 42
 <212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (42)
<223> Kaa equals stop translation
<400> 194
Met Pro Thr Ile Trp Val Lys Leu Cys Leu Leu Gln Val Cys His Gly
1 5 10 15
Leu Phe Pro Leu Leu Lys His Trp Ser Gln Pro Met Pro Leu Cys Val
Thr Leu Ala Pro Val Ser Tyr Trp Leu Xaa 35 40
<210> 195
<211> 260
<212> PRT
<213> Homo sapiens
<220×
<221> SITE
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<222> (260)

<223> Xaa equals stop translation

Met Gly Thr Ala Ala Leu Gly Pro Val Trp Ala Ala Leu Leu Phe 1 5 10 15

Leu Leu Met Cys Glu Ile Pro Met Val Glu Leu Thr Phe Asp Arg Ala 20 25 30

Val Ala Ser Asp Cys Gln Arg Cys Cys Asp Ser Glu Asp Pro Leu Asp 35 40 45

Pro Ala His Val Ser Ser Ala Ser Ser Ser Gly Arg Pro His Ala Leu 50 55 60

Pro Glu Ile Arg Pro Tyr Ile Asn Ile Thr Ile Leu Lys Gly Asp Lys 65 70 75 80

Gly Asp Pro Gly Pro Met Gly Leu Pro Gly Tyr Met Gly Arg Glu Gly 85 90 95

Pro Gln Gly Glu Pro Gly Pro Gln Gly Ser Lys Gly Asp Lys Gly Glu
100 105 110

Met Gly Ser Pro Gly Ala Pro Cys Gln Lys Arg Phe Phe Ala Phe Ser 115 120 125

Val Gly Arg Lys Thr Ala Leu His Ser Gly Glu Asp Phe Gln Thr Leu 130 135 140

Leu Phe Glu Arg Val Phe Val Asn Leu Asp Gly Cys Phe Asp Met Ala 145 150 155 160

Thr Gly Gln Phe Ala Ala Pro Leu Arg Gly Ile Tyr Phe Phe Ser Leu 165 170 170

Asn Val His Ser Trp Asn Tyr Lys Glu Thr Tyr Val His Ile Met His 180 185 190

Asn Gln Lys Glu Ala Val Ile Leu Tyr Ala Gln Pro Ser Glu Arg Ser 195 200 205

Ile Met Gln Ser Gln Ser Val Met Leu Asp Leu Ala Tyr Gly Asp Arg 210 215 220

Val Trp Val Arg Leu Phe Lys Arg Gln Arg Glu Asn Ala Ile Tyr Ser 225 230 235 240

Asn Asp Phe Asp Thr Tyr Ile Thr Phe Ser Gly His Leu Ile Lys Ala

Clu Asp Asp Xaa 260

<210> 196

<211> 117

<212> PRT

<213> Homo sapiens

Met Leu Gly His Cys Cys Tyr Phe Trp Gln Val Trp Pro Ala Ser Glu
1 5 10 15

Ala Leu Ala Ala Gly Pro Thr Pro Ser Thr Gly Ser Ser Ser Pro Ser 20 25 30

Trp Lys Gln His Ile Gly Thr Ser Leu Gln Lys Thr Arg Gly Ser Leu 35 40 45

Pro Thr Thr Leu Thr Ser Gly Ala Gly Gln Ser Thr Ser Thr Gly 50  $\phantom{000}55\phantom{000}$ 

Lys Asn Pro Ala Ala Gly Arg Ser Leu Glu Gly Ala Leu Pro Ala Gly 65  $70_{\odot}$  75 80

Val Trp Pro Cys Phe Ala Gln Ser Pro Cys Thr Gly Gly Gln Gln Thr 85 90 95

Pro Ser Ser Thr Gly Leu Arg Ser Cys Leu Val Arg Ser Pro Ala Thr

Trp Trp Arg Thr Pro 115

<210> 197 <211> 698

<212> PRT

<213> Homo sapiens

Met Leu Pro Ala Arg Leu Pro Phe Arg Leu Leu Ser Leu Phe Leu Arg 1 5 10 15

Gly Ser Ala Pro Thr Ala Ala Arg His Gly Leu Arg Glu Pro Leu Leu 20 - 25 30

Glu Arg Arg Cys Ala Ala Ala Ser Ser Phe Gln His Ser Ser Ser Leu  $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45 \hspace{1.5cm}$ 

Gly Gly Asp Met Gln Glu Arg Phe Leu Phe Pro Glu Tyr Ile Leu Asp 65 70 75 80

Pro Glu Pro Gln Pro Thr Arg Glu Lys Gln Leu Gln Gln Gln Gln 95

Gln Gln Glu Glu Glu Arg Gln Arg Gln Gln Arg Arg Glu Glu Arg 100 105 110

Arg Gln Gln Asn Leu Arg Ala Arg Ser Arg Glu His Pro Val Val Gly 115 120 125

His Pro Asp Pro Ala Leu Pro Pro Scr Gly Val Asn Cys Ser Gly Cys

	130	1				139	5				140	)			
Gly 145	Ala	Glu	Leu	His	Cys 150	Gl:	a Asg	Ala	Gl <sub>3</sub>	y Va:		Gly	<b>ሃ</b> ፒሂ፣	Lei	1 Pro
Arg	Glu	Lys	Phe	165	Arg	Thi	r Ala	Glu	170	Ası	Gly	/ Gly	/ Let	1 Ala 179	
Thr	Val	Суз	Gln 180	Arg	Cys	Tr	) Leu	185	Ser	His	His	Arç	190		Leu
Arg	Leu	Gln 195	Val	Ser	Arg	Glu	200	Tyr	Leu	Glu	ı Leu	Val 205		Ala	Ala
	210					215					220	)			
225					230		Pro			235	•				240
				245			<b>A</b> sn		250	ľ				255	i
			250				Leu	265		•			270		
		275					Ala 280					285			
	290					295					300				
305					310		Asp			315					320
				325			Ile		330					335	
			340				Val	345					350		
		355					Glu 360					365			
	373					375	Thr				38Ò		•		
202					390		Ile			395					400
				405			Lys		410					415	
			420				Asn	425					430		
Gly	Tyr	Val 435	Val	Gly	Arg	Val	Gly 440	Arg	Thr	Phe	Leu	Tyr 445	Ser	Glu	Glu

Gln Lys Asp Asn Ile Pro Phe Glu Phe Asp Ala Asp Ser Leu Ala Phe 450 455 460

Asp Met Glu Asn Asp Pro Val Met Gly Thr His Lys Ser Thr Lys Gln 465 470 475 480

Val Glu Leu Thr Ala Gln Asp Val Lys Asp Ala His Trp Phe Tyr Asp 485 490 495

Thr Pro Gly Ile Thr Lys Glu Asn Cys Ile Leu Asn Leu Leu Thr Glu 500 505 Leu Asn Leu Thr Glu

Lys Glu Val Asn Ile Val Leu Pro Thr Gln Ser Ile Val Pro Arg Thr 515 520 525

Phe Val Leu Lys Pro Gly Met Val Leu Phe Leu Gly Ala Ile Gly Arg 530 535 540

Ile Asp Phe Leu Gln Gly Asn Gln Ser Ala Trp Phe Thr Val Val Ala 545 550 550 560

Ser Asn Ile Leu Pro Val His Ile Thr Ser Leu Asp Arg Ala Asp Ala 565 570 575

Leu Tyr Gln Lys His Ala Gly His Thr Leu Leu Gln Ile Pro Met Gly 580 590

Gly Lys Glu Arg Met Ala Gly Phe Pro Pro Leu Val Ala Glu Asp Ile 595 600 605

Met Leu Lys Glu Gly Leu Gly Ala Ser Glu Ala Val Ala Asp Ile Lys 610 615 620

Phe Ser Ser Ala Gly Trp Val Ser Val Thr Pro Asn Phe Lys Asp Arg 625 630 635 640

Leu His Leu Arg Gly Tyr Thr Pro Glu Gly Thr Val Leu Thr Val Arg 645 650 655

Pro Pro Leu Leu Pro Tyr Ile Val Asn Ile Lys Gly Gln Arg Ile Lys 660 665 670

Lys Ser Val Ala Tyr Lys Thr Lys Lys Pro Pro Ser Leu Met Tyr Asn 675 680 685

Val Arg Lys Lys Lys Gly Lys Ile Asn Val 690 695

<210> 198

<211> 348

<212> PRT

<213> Homo sapiens

Met Asr Met Thr Gln Ala Arg Val Lou Val Ala Ala Val Val Gly Leu 1 5 10 15

Val Ala Val Leu Leu Tyr Ala Ser Ile His Lys Ile Glu Glu Gly His

			20	0				25	5				3 (	)	
Leu	Ala	Val	Ту	с Туг	Arg	Gly	Gly 40	Ala	Let	ı Lev	Thr	Se:		Sei	Gly
Pro	Gly 50	Тух	His	s Ile	Met	Leu 55	Pro	Phe	lle	Thr	Thr 60		arg	Ser	. Val
G1n 65	Thr	Thr	Leu	ı Glm	Thr 70	Asp	Glu	Val	. Lys	Asn 75		Pro	Суз	Gly	Thr 80
Ser	Gly	Gly	Val	. Met 85	Ile	Tyr	Ile	Asp	Arg 90	Ile	Glu	Val	Val	Asn 95	
Leu	Ala	Pro	Туг 100	Ala	Val	Phe	Asp	Ile 105	Val	Arg	Asn	Tyr	Thx 110		Asp
<b>ጉ</b> ሃድ	Asp	Lys 115	Thr	Leu	Ile	Phe	Asn 120	Lys	Ile	His	His	Glu 125	Leu	Asn	Gln
Phe	Cys 130	Ser	Ala	His	Thr	Leu 135	G1n	Glu	Val	Tyr	Ile 140	Glu	Leu	Phe	Asp
Gln 145	Ile	Asp	Glu	Asn	Leu 150	Lys	Gln	Ala	Leu	Gln 155	Lys	Asp	Leu	Asn	Leu 160
				Leu 165					170					175	_
Ile	Pro	Glu	Ala 180	Ile	Arg	Arg	Asn	Phe 185	Glu	Leu	Met	Glu	Ala 190	Glu	Lys
Thr	Lys	Leu 195	Leu	Ile	Ala	Ala	Gln 200	Lys	Gln	Lys	Val	Val 205	Glu	Lys	Glu
Ala	Glu 210	Thr	Glu	Arg	Lys	Lys 215	Ala	Val	Ile	Glu	Ala 220		Lys	Ile	Ala
31n 225	Val	Ala	Lys	rle	Arg 230	Phe	Gln	Gİn	Lys	Val 235	Met	Glu	Lys	Glu	Thr 240
Glu	Lys	Arg	Ile	Ser 245	Glu	Ile	Glu	qeA	Ala 250	Ala	Phe	Leu	Ala	Arg 255	Glu
Lys	Ala	Lys	Ala 260	Asp	Ala	Glu	Туг	Tyr 265	Ala	Ala	His	Lys	туr 270	Ala	Thr
Ser	nek	Lys 275	His	Lys	Leu	Thr	Pro 280	Glu	Tyr	Leu	Glu	Leu 285	Lys	Lys	Tyr
In	Ala 290	Ile	Ala	Ser	Asn	Ser 295	Lys	Ile	Ţуr		Gly 300	Ser	Asn	Ile	Pro
Asn 805	Ne:	Phe	Val	Ąsp	Ser 310	Ser	Cys	λla	Leu	Lys 315	Tyr	Ser	Asp	Ile	Arg 320
hr	Gly	Arg	Glu	Ser 325	Ser !	Leu	Pro	Ser	Lys 330	Glu .	Ala	Leu		Pro 335	Ser

Gly Glu Asn Val Ile Gln Asn Lys Glu Ser Thr Gly 340

<210> 199

<211> 401

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (307)

<223> Xaa equals any of the naturally occurring L-amino acids

Met Met Gly Leu Gly Asn Gly Arg Arg Ser Met Lys Ser Pro Pro Leu

1 5 10 15

Val Leu Ala Ala Leu Val Ala Cys Ile Ile Val Leu Gly Phe Asn Tyr 20 25 30

Trp Ile Ala Ser Ser Arg Ser Val Asp Leu Gin Thr Arg Ile Met Glu 35 40 45

Leu Glu Gly Arg Val Arg Arg Arg Ala Ala Glu Arg Gly Ala Val Glu 50 60

Leu Lys Lys Asn Glu Phe Gln Gly Glu Leu Glu Lys Gln Arg Glu Gln 65 70 75 80

Leu Asp Lys Ile Gln Ser Ser His Asn Phe Gln Leu Glu Ser Val Asn 85 90 95

Lys Leu Tyr Gln Asp Glu Lys Ala Val Leu Val Asn Asn Ile Thr Thr 100 105 110

Gly Glu Arg Leu Ile Arg Val Leu Gln Asp Gln Leu Lys Thr Leu Gln 115 120 125

Arg Asn Tyr Gly Arg Leu Gln Gln Asp Val Leu Gln Phe Gln Lys Asn 130 135 140

Gln Thr Asn Leu Glu Arg Lys Phe Ser Tyr Asp Leu Ser Gln Cys Ile 145 150 155 160

Asn Gin Met Lys Glu Val Lys Glu Gln Cys Glu Clu Arg Ile Glu Glu 165 170 175

Val Thr Lys Lys Gly Asn Glu Ala Val Ala Ser Arg Asp Leu Ser Glu 180 185 190

Asn Asn Asp Gln Arg Gln Gln Leu Gln Ala Leu Ser Glu Pro Gln Pro 195 200 205

Arg Leu Gln Ala Ala Gly Leu Pro His Thr Glu Val Pro Gln Gly Lys 210 220

Gly Asn Val Leu Gly Asn Ser Lys Ser Gln Thr Pro Ala Pro Ser Ser 225 230 235 240

Glu Val Val Leu Asp Ser Lys Arg Gln Val Glu Lys Glu Glu Thr Asn

Glu Ile Gln Val Val Asn Glu Glu Pro Gln Arg Asp Arg Leu Pro Glr. 260 265 270

Glu Pro Gly Arg Glu Gln Val Val Glu Asp Arg Pro Val Gly Gly Arg 275 280 285

Gly Phe Gly Gly Ala Gly Glu Leu Gly Gln Thr Pro Gln Val Gln Ala 290 295 300  $\cdot$ 

Ala Leu Xaa Val Ser Gin Glu Asn Pro Glu Met Glu Gly Pro Glu Arg 305 310 315 .320

Asp Gln Leu Val Ile Pro Asp Gly Gln Glu Glu Glu Gln Glu Ala Ala 325 330 335

Gly Glu Gly Arg Asn Gln Gln Lys Leu Arg Gly Glu Asp Asp Tyr Asn 340 345 350

Net Asp Glu Asn Glu Ala Glu Ser Glu Thr Asp Lys Gln Ala Ala Leu 355 360 365

Ala Gly Asn Asp Arg Asn Ile Asp Val Phe Asn Val Glu Asp Gln Lys 370 375 380

Arg Asp Thr Ile Asn Leu Leu Asp Gln Arg Glu Lys Arg Asn His Thr  $385^{\circ}$  390 395 400

<210> 200

<211> 324 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 200

Met Glu Xaa Ala Lys Val Tyr Val Ala Lys Val Asp Cys Thr Ala His 1 5 10 15

Ser Asp Val Cys Ser Ala Gln Cly Val Arg Gly Tyr Pro Thr Leu Lys

Leu Phe Lys Pro Gly Gln Glu Ala Val Lys Tyr Gln Gly Pro Arg Asp 35 40 . 45

Phe Gln Thr Leu Glu Asn Trp Met Leu Gln Thr Leu Asn Glu Glu Pro 50 55 60

Val Thr Pro Glu Pro Glu Val Glu Pro Pro Ser Ala Pro Glu Leu Lys.

69	5				70	)				75	i				80
Glr	ı Gly	/ Let	ı Tyı	61 Glu	ı Leu	Set	Ala	ı Sei	Asn 90	Phe	Glu	Leu	His	Val 95	Ala
Glr	Gly	/ Asp	100	Phe	lle	Lys	Phe	Phe 105	Ala	Pro	Trp	Cys	Gly 110		Сує
ГÀЗ	Ala	Let 119	Ala S	Pro	Thr	Trp	Glu 120	Glr	Leu	Ala	Leu	Gly 125		Glu	His
Ser	Glu 130	Thr	· Val	Lys	Ile	Gly 135	Lys	Val	Asp	Cys	Thr 140	Gln	His	Tyr	Glu
Leu 145	Суз	Ser	Gly	Asn	Gln 150	Val	Arg	Gly	Tyr	Pro 155	Thr	Leu	Leu	Trp	Phe 160
Arg	Asp	Gly	Lys	Lys 165	Val	Asp	Gln	Туr	Lys 170	Gly	Lys	Arg	Asp	Leu 175	Glu
Ser	Leu	Arg	Glu 180	Tyr	Val	Glu	Ser	Gln 185	Leu	Gln	Arg	The	Glu 190	Thr	Gly
Ala	Thr	Glu 195	Thr	Val	Thr	Pro	Ser 200	Glu	Ala	Pro	Val	Leu 205	Ala	Ala	Glu
Pro	Glu 210	Ala	Asp	Lys	Gly	Thr 215	Val	Leu	Ala	Leu	Thr 220	Glu	Asn	Asn	Fhe
Asp 225	Asp	Thr	Ile	Ala	Glu 230	Gly	Ile	Thr	Phe	Ile 235	Lys	Phe	Tyr	Ala	Pro 240
Trp	Суэ	Gly	His	Cys 245	Lys	Thr	Leu	Ala	Pro 250	Thr	Trp	Glu	Glu	Leu 255	Ser
Lys	Lys	Glu	Phe 260	Pro	Gly	Leu	Ala	Gly 265	Val	Lys	Ile	Ala	Glu 270	Val	Asp
Cys	Thr	Ala 275	Glu	Arg	Asn <sub>.</sub>	Ile	Cys 280	Ser	Lys	Tyr		Val 285	Arg	Gly	Tyr
Pro	Thr 290	Leu	Leu	Leu	Phe	Arg 295	Gly	Gly	Lys	Lys	Val 300	Ser	G1u	His	Ser
Gly 305	Gly	Arg	Asp	Leu	Asp 310	Ser	Leu	His	Arg	Phe 315	Val	Leu	Ser		Ala 320
ГЛЭ	qeA	Glu	Leu				•								
<210> 201 <211> 90 <212> PRT <213> Homo sapiens															

Ser Pro Val Leu Arg Ala Leu Ala Ala Ser Cys Leu Ala Ser Pro Ala 20 25 30

Gly Cys Cys Gly Thr Arg Lys Ala Leu Asn Gly Asn Val Gly Glu Lys  $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$ 

Val Gly Phe Thr Phe Net Ser Phe Gln Gly Cys Asp Pro Ser Ser Pro 50 55 60

Gly Cys Leu Cys Cys Ser Leu Leu Pro Ser Asn Ser Gln Leu Val Phe 65 70 75 80

Ile Ser Phe Leu Val Leu Ser Gly Leu Ala 85 90

<210> 202

<211> 243 <212> PRT

<213> Homo sapiens

Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu Arg Gly Leu  $1 \ 5 \ 10 \ 15$ 

Leu Leu Leu Leu Leu Cln Leu Pro Ala Pro Ser Ser Ala Ser Glu 20 25 30

Ile Pro Lys Gly Lys Gln Lys Ala Gln Leu Arg Gln Arg Glu Val Val 35 40 45

Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro Gly 50 60

Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile 65 70 75 80

Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg Glu 85 90 95

Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp Ser 100 105 110

Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr Phe 115 120 125

Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly Ser 130 135 140

Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile 165 170 175

Tyr Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His 180 185 190

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Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu 195 200 205 Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly 210 215 220 Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu 225 230 235 240 Leu Pro Lys <210> 203 <211> 75 <212> PRT <213> Homo sapiens Met Ala Cly Gln Glu Asp Pro Val Gln Arg Glu Ile His Gln Asp Trp 1 5 10 15 Ala Asn Arg Glu Tyr Ile Glu Ile Ile Thr Ser Ser Ile Lys Lys Ile
20 25 30 Ala Asp Phe Leu Asn Ser Phe Asp Met Ser Cys Arg Ser Arg Leu Ala  $\begin{bmatrix} 35 \\ \end{bmatrix}$ Thr Leu Asn Glu Lys Leu Thr Ala Leu Glu Arg Arg Ile Glu Tyr Ile Glu Ala Arg Val Thr Lys Gly Glu Thr Leu Thr 65 70 75 <210> 204 <211> 248 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (185) <223> Xaa equals any of the naturally occurring L-amino acids <400> 204 Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Ile Lys Val Ile 35 40 45

Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser

Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile 50 55 60

65 70 80 Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Phe Phe Phe Ile 85 90 95 Ile Ser Gly Ser Leu Ser Ile Ala Thr Glu Lys Arg Leu Thr Lys Leu 100 105 110 Leu Val His Ser Ser Leu Val Gly Ser Ile Leu Ser Ala Leu Ser Ala 115 120 125 Leu Val Gly Phe Ile Ile Leu Sor Val Lys Gln Ala Thr Leu Asn Pro 130 135 140 Ala Ser Leu Gln Cys Glu Leu Asp Lys Asn Asn Ile Pro Thr Arg Ser 145 150 155 160 Tyr Val Ser Tyr Phe Tyr His Asp Ser Leu Tyr Thr Thr Asp Cys Tyr 165 170 175 Thr Ala Lys Ala Ser Leu Ala Gly Xaa Leu Ser Leu Met Leu Île Cys 180 185 190 Thr Leu Leu Glu Phe Cys Leu Ala Val Leu Thr Ala Val Leu Arg Trp 195 200 205 Lys Gln Ala Tyr Scr Asp Phe Pro Gly Ser Val Leu Phe Leu Pro His 210 215 Ser Tyr Ile Gly Asn Ser Gly Met Ser Ser Lys Met Thr His Asp Cys 225 230 240 Gly Tyr Glu Glu Leu Leu Thr Ser <210> 205 <211> 168 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (83) <223> Xaa equals any of the naturally occurring L-amino acids <400> 205 Het Pro Leu Leu Arg Gly Leu Leu Trp Leu Gln Val Leu Cys Ala Gly
1 5 10 15 Pro Leu His Thr Glu Ala Val Val Leu Leu Val Pro Ser Asp Asp Gly
20 25 30 Arg Ala Phe Leu Leu Arg Ser Arg Leu Leu His Pro Glu Ala His Val Pro Pro Ala Ala Asp Arg Gly Ala Ser Leu Gln Cys Val Leu His Gln 50 55 60

Ala Ala Pro Lys Ser Arg Pro Arg Ser Pro Ala Ala Gly Ala Ala Leu 65 70 75 80

Leu His Xaa Pro Arg Arg Thr Gly Asp Glu Pro Cys Arg Glu Phe His 85 90 95

Gly Asn Gly Phe Pro Gly Pro Thr Gln Leu Thr Pro Gly Glu Cys Gly 100 105 110

Leu Pro Ala Pro Ser Ser Leu Leu Gln His Ala Ser Ala Pro Val Arg 115 120 125

Thr Gly Ser Glu Gly Gln Val Val Gly Cys Pro Arg Ala Arg Gly Glu 130 135 140

Ser Arg Asn Gly Leu Val Gly Cys 165

<210> 206

<211> 218

<212> PRT

<213> Homo sapiens

<400> 206

Met Gly Ser Ala Ala Leu Glu Ile Leu Gly Leu Val Leu Cys Leu Val 1 5 10 15

Gly Trp Gly Gly Leu IIe Leu Ala Cys Gly Leu Pro Met Trp Gln Val  $20 \\ 25 \\ 30$ 

Thr Ala Phe Leu Asp His Asn Ile Val Thr Ala Gln Thr Thr Trp Lys

Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly His Met Gln Cys
50 55 60

Lys Val Tyr Asp Ser Val Leu Ala Leu Ser Thr Glu Val Gln Ala Ala 65 70 75 80

Arg Ala Leu Thr Val Ser Ala Val Leu Leu Ala Phe Val Ala Leu Phe 85 90 95

Val Thr Leu Ala Gly Ala Gln Cys Thr Thr Cys Val Ala Pro Gly Pro 100 105 110

Ala Lys Ala Arg Val Ala Leu Thr Gly Gly Val Leu Tyr Leu Phe Cys 115 120 125

Gly Leu Leu Ala Leu Val Pro Leu Cys Trp Phe Ala Asn Ile Val Val 130 135 140

Arg Glu Phe Tyr Asp Pro Ser Val Pro Val Scr Gln Lys Tyr Glu Leu 145 150 155 . 160

Gly Ala Ala Leu Tyr Ile Gly Trp Ala Ala Thr Ala Leu Leu Met Val

Gly Gly Cys Leu Leu Cys Cys Gly Ala Trp Val Cys Thr Gly Arg Pro 180 185 190 Asp Leu Ser Phe Pro Val Lys Tyr Ser Ala Pro Arg Arg Pro Thr Ala 195 200 205

Thr Gly Asp Tyr Asp Lys Lys Asn Tyr Val 210 215

<210> 207 <211> 73 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (73)

<223> Xaa equals stop translation

<400> 207

Met Thr Ser Tyr Ile Leu Ile Ser Phe Val Leu Leu Ile Gly Val Gly
1 5 10 15

Cys Ile Glu Lys Asp Gln Ser Cys Pro Val Phe Gly Gly Arg Lys Arg 20 25 30

Leu His Leu Leu Phe Val Gly Gly Gln Leu Arg Gln Val Arg Met Leu  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Arg Gly Glu Leu Ser Cys Ala Cys Tyr Arg Pro His Val Gln Ala Leu  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Gin Leu Gly Gly Cys Thr Cys Phe Xaa 65

<210> 208 <211> 348

<212> PRT

<213> Homo sapiens

<400> 208

Met Leu Cys Pro Trp Arg Thr Ala Asn Leu Gly Leu Leu Leu Ile Leu 1 5 10 15

Thr Ile Phe Leu Val Ala Glu Ala Glu Gly Ala Ala Gln Pro Asn Asn 20 25 30 .

Ser Leu Met Leu Gln Thr Ser Lys Glu Asr. His Ala Leu Ala Ser Ser 35 40 45

Ser Leu Cys Met Asp Glu Lys Gln Ile Thr Gln Asn Tyr Ser Lys Val

Leu Ala Glu Val Asn Thr Ser Trp Pro Val Lys Met Ala Thr Asr. Ala 65 70 75 80

Val	Leu Cys Cys	Pro	Pro	Ile A	Ala	Leu	Arg	Asn	Leu	Ile	Ile	Ile	Thr
		85					90					95	

- Trp Glu Ile Ile Leu Arg Gly Gln Pro Ser Cys Thr Lys Ala Tyr Lys 100 105 110
- Lys Glu Thr Asn Glu Thr Lys Glu Thr Asn Cys Thr Asp Glu Arg Ile 115 120 125
- Thr Trp Val Ser Arg Pro Asp Gln Asn Ser Asp Leu Gln Ile Arg Thr 130 135 140
- Val Ala Ile Thr His Asp Gly Tyr Tyr Arg Cys Ile Met Val Thr Pro 145 150 155 160
- Asp Gly Asn Phe His Arg, Gly Tyr His Leu Gln Val Leu Val Thr Pro 165 170 175
- Glu Val Thr Leu Phe Gln Asn Arg Asn Arg Thr Aia Val Cys Lys Ala 180 185 190
- Val Ala Gly Lys Pro Ala Ala His Ile Ser Trp Ile Pro Glu Gly Asp 195 . . . 200 205
- Cys Ala Thr Lys Gln Glu Tyr Trp Ser Asn Gly Thr Val Thr Val Lys 210 215 220
- Ser Thr Cys His Trp Glu Val His Asn Val Ser Thr Val Asn Cys His 225  $230^{\circ}$  235 240
- Val Ser His Leu Thr Gly Asn Lys Ser Leu Tyr Ile Glu Leu Leu Pro 245 250 255
- Val Pro Gly Ala Lys Lys Ser Ala Lys Leu Tyr Ile Pro Tyr Ile Ile 260 265 270
- Leu Thr Ile Ile Ile Leu Thr Ile Val Gly Phe Ile Trp Leu Leu Lys 275 280 285
- Val Asn Gly Cys Arg Lys Tyr Lys Leu Asn Lys Thr Glu Ser Thr Pro 290 295 300
- Val Val Glu Glu Asp Glu Met Gln Pro Tyr Ala Ser Tyr Thr Glu Lys 305 310 315 320
- Asn Asn Pro Leu Tyr Asp Thr Thr Asn Lys Val Lys Ala Ser Glu Ala 325 \$330\$
- Leu Gln Ser Glu Val Asp Thr Asp Leu His Thr Leu 340 345

<210> 209 <211> 73

<212> PRT

<213> Homo sapiens

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<221> SITE
 <222> (73)
 <223> Xaa equals stop translation
 Met Ala Arg Gly Cys Val Cys Ser Leu Cys Ala Ser Val Cys Ile Phe
1 5 10 15
 Leu Ser Ser Leu Phe Pro Leu Leu Pro Ser Val His Ser Val Asn Ile
20 25 30
 Ile Ser Cys Leu Leu Ser Lys Cys Phe Glu Gly Leu Glu Leu Met
Cys Glu His Leu Tyr Gln Leu Ser Gln Leu His Val Leu His His Ile 50 55 60
Phe Ser Tyr Leu Leu Cys Thr Pro Xaa 65 70
<210> 210
<211> 608
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (265)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (597)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 210
Met Val Gly Thr Lys Leu Arg Gln Thr Lys Asp Ala Leu Phe Thr Ile
1 5 10 15
Leu His Asp Leu Arg Pro Gln Asp Arg Phe Ser Ile Ile Gly Phe Ser 20 25 30
Asn Arg Ile Lys Val Trp Lys Asp His Leu Ile Ser Val Thr Pro Asp 35 40 45
Ser Ile Arg Asp Gly Lys Val Tyr Ile His His Met Ser Pro Thr Gly 50 \hspace{1cm} 55 \hspace{1cm} 60
Gly Thr Asp Ile Asm Gly Val Leu Gln Arg Ala Ile Arg Leu Leu Asm 65 70 75 80
Lys Tyr Val Ala His Ser Gly Ile Gly Asp Arg Ser Val Ser Leu Ile
85 90 95
```

Val Phe Leu Thr Asp Gly Lys Pro Thr Val Gly Glu Thr His Thr Leu 100 105 110

Lys Ile Leu Asn Asn Thr Arg Glu Ala Ala Arg Gly Gln Val Cys Ile

		TI	•				120	)				12	5		
Phe	Th:	r Ile	e Gly	/ Ile	e Gly	/ Asr 135	n Ası	Va.	l Ası	p Ph	e Arg	g Le	u Lei	ı Glı	u Ly
Let 145	Sei	Leu	ı Glu	ı Aşr	150	Gly	/ Lei	ı Thi	Arg	15	g Val	l Hi:	s Glu	ı Glı	u Gl 16
Ast	Ala	Gly	/ Ser	Gln 165	Leu	Ilc	Gly	Phe	170	r Ası	p Glu	ı 11e	e Arg	Th:	
Leu	Leu	Ser	180	Ile	Arg	Ile	Asp	Tyr 185	Pro	Pro	Ser	Sei	val 190		l Gl
Ala	Thr	Lys 195	Thr	Leu	Phe	Pro	Asn 200	Туг	Phe	e Asr	ı Gly	205		Ile	2 II
Ile	Ala 210	Gly	Lys	Leu	Val	Asp 215	Arg	Lys	Leu	Asp	220	Leu	His	Val	Glı
Val 225	Thr	Ala	Ser	Asn	Ser 230	Lys	Lys	Phe	Ile	11e 235	e Leu	Lys	Thr	Asp	Val 240
Pro	Val	Arg	Pro	Gln 245	Lys	Ala	Gly	Lys	Asp 250	Val	. Thr	Gly	Ser	Pro 255	Arg
Pro	Gly	Gly	Asp 260	Gly	Glu	Gly	Asp	Xaa 265	Asn	His	Ile	Glu	Arg 270	Leu	Tr
Ser	Tyr	Leu 275	Thr	Thr	Lys	Glu	Leu 280	Leu	Ser	Ser	Trp	Leu 285		Ser	Asp
Asp	Glu 290	Pro	Glu	Lys	Glu	Arg 295	Leu	Arg	Gln	Arg	Ala 300	Gln	Ala	Leu	Ala
305					310					315					320
				325					330		His			335	
Ala	Met	Gly	Pro 340	Glu	Pro	Val	Val	Gln <b>34</b> 5	Ser	Val	Arg	Gly	Ala 350	Gly	Thr
3ln	Pro	Gly 3 <b>5</b> 5	Pro	Leu	Leu	Lys	Lys 360	Pro	Tyr	Gln	Pro	Arg 365	Ile	Lys	Ile
er	Lys 370	Thr	Ser	Val	Asp	Gly 375	Asp	Pro	His	Phe	Val 380	Val	Asp	Phe	Pro
eu 185	Ser	Arg	Leu	Thr	Val 390	Cys	Phe	Asn	Ile	Asp 395	Gly	Gln	Pro	Gly	Asp 400
1e	Leu	Arg	Leu	Val 4C5	Ser .	Asp	His	Arg	Asp 410	Ser	Gly	Val	Thr	Val 415	Asa
1y	Glu	Leu	Ile 420	Gly	Ala	Pro	Ala	Pro 425	Pro	Asn	Gly	His	Lys 430	Lys	Gln

Arg Thr Tyr Leu Arg Thr Ile Thr Ile Leu Ile Asn Lys Pro Glu Arg 415 440 445 .

Ser Tyr Leu Glu Ile Thr Pro Ser Arg Val Ile Leu Asp Cly Gly Asp 450 455 460

Arg Leu Val Leu Pro Cys Asn Gln Ser Val Val Val Gly Ser Trp Gly 465 470 480

Leu Glu Val Ser Val Ser Ala Asn Ala Asn Val Thr Val Thr Ile Gln 485 490 495

Gly Ser Ile Ala Phe Val Ile Leu Ile His Leu Tyr Lys Lys Pro Ala 500 505 510

Pro Phe Gln Arg His His Leu Gly Phe Tyr Ile Ala Asn Ser Glu Gly 515 520 525

Lou Ser Ser Asn Cys His Gly Leu Leu Gly Gln Phe Leu Asn Gln Asp 530 535 540

Ala Arg Leu Thr Glu Asp Pro Ala Gly Pro Ser Gln Asn Leu Thr His 545 550 555 556

Pro Leu Leu Cur Gln Val Gly Glu Gly Pro Glu Ala Val Leu Thr Val 565 570 570

Lys Gly His Gln Val Pro Val Val Trp Lys Gln Arg Lys Ile Tyr Asn 580 585 590

Gly Glu Glu Gln Xaa Asp Cys Trp Phe Ala Arg Asn Met Pro Pro Asn 595 600 605

<210> 211

<211> 252

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (252)

<223> Xaa equals stop translation

<400> 211

Met Ala Pro Ala Ser Arg Leu Leu Ala Leu Trp Ala Leu Ala Ala Val 1 5 10 15

Ala Leu Pro Gly Ser Gly Ala Glu Gly Asp Gly Gly Trp Arg Pro Gly 20 25 30

Gly Pro Gly Ala Val Ala Glu Glu Glu Arg Cys Thr Val Glu Arg Arg 35 40 45

Ala Asp Leu Thr Tyr Ala Glu Phe Val Glr Gln Tyr Ala Phe Val Arg 50 55 60

Pro Val Ile Leu Gln Gly Leu Thr Asp Asn Ser Arg Phe Arg Ala Leu 65 70 75 80

Cys Ser Arg Asp Arg Leu Leu Ala Ser Phe Gly Asp Arg Val Val Arg 85 90 95

Leu Ser Thr Ala Asn Thr Tyr Ser Tyr His Lys Val Asp Leu Pro Phe 100 105 110

Gln Glu Tyr Val Glu Gln Leu Leu His Pro Gln Asp Pro Thr Ser Leu 115 120 125

Gly Asn Asp Thr Leu Tyr Phe Phe Gly Asp Asn Asn Phe Thr Glu Trp 130 135 140

Ala Ser Leu Phe Arg His Tyr Ser Pro Pro Pro Phe Gly Leu Leu Gly 145 155 160

Thr Ala Pro Ala Tyr Ser Phe Gly Ile Ala Gly Aia Gly Ser Gly Val 165 170 175

Pro Phe His Trp His Gly Pro Gly Tyr Ser Glu Val Ile Tyr Gly Arg

Lys Arg Trp Phe Leu Tyr Pro Pro Glu Lys Thr Pro Glu Phe His Pro 195 200 205

Asn Lys Thr Thr Leu Ala Trp Leu Arg Asp Thr Tyr Pro Ala Cys Thr 210 215 220

Val Cys Thr Ala Leu Glu Cys Thr Ile Arg Ala Gly Glu Val Leu Thr 225 230 235 240

Ser Arg Pro Leu Val Ala Cys Tyr Ala Gln Pro Xaa

<210> 212

<211> 226

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (226)

<223> Xaa equals stop translation

<400> 212

Met Lys Glu Ile Pro Ala Leu Leu His Leu Pro Val Leu Ile Ile Met 1 . 5 10 15

Val Leu Arg His Ile Gly Gly Pro Glu Arg Glu Pro Pro Glr. Ala Leu  $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$ 

Arg Pro Arg Asp Arg Arg Gln Glu Glu Ile Asp Tyr Arg Pro Asp

Gly Gly Ala Gly Asp Ala Asp Phe His Tyr Arg Gly Gln Met Gly Pro 65 70 75 80 Thr Glu Gln Gly Pro Tyr Ala Lys Thr Tyr Glu Gly Arg Arg Glu Ile 85 90 95 Leu Arg Glu Arg Asp Val Asp Leu Arg Phe Gln Thr Gly Asn Lys Ser 100 105 110Pro Glu Val Leu Arg Ala Phe Asp Val Pro Asp Ala Glu Ala Arg Glu 115 120 125 His Pro Thr Val Val Pro Ser His Lys Ser Pro Val Leu Asp Thr Lys Pro Lys Glu Thr Gly Gly Tie Leu Gly Glu Gly Thr Pro Lys Glu Ser 145 155 160 Ser Thr Glu Ser Ser Gln Ser Ala Lys Pro Val Ser Gly Gln Asp Thr 165 170 175 Ser Gly Asn Thr Glu Gly Ser Pro Ala Ala Glu Lys Ala Gln Leu Lys 180 185 190 Ser Glu Ala Ala Gly Ser Pro Asp Gln Gly Ser Thr Tyr Ser Pro Ala 195 200 205 Arg Cly Val Ala Cly Pro Arg Cly Gln Asp Pro Val Ser Ser Pro Cys 210 215 220**Gly** Xaa <210> 213 <211> 51 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (51) <223> Xaa equals stop translation Met Met Gly Leu Leu Glu Thr Gly Asn Val Leu Phe Trp Val Trp Val 1 5 10 15 Val Val Thr Cys Val Tyr Ser Leu Tyr Ala Asn Ser Leu Asn Cys Thr 20 25 30

Asp Met Asp Cys Ala Pro Phe Tyr Met Cys Val Met Leu Gln Gln Lys  $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$ 

Cys Gln Xaa 50

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<210> 214
 <211> 172
<212> PRT
  <213> Homo sapiens
  <220>
 <221> SITE
  <222> (172)
  <223> Xaa equals stop translation
 <400> 214
 Met Trp Leu Trp Ala Val Ser Pro Val Arg Pro Arg Thr Cys Leu Pro
1 5 10 15
 Pro Cys Pro Arg Leu Trp Leu Trp Ile Ser Met Thr Leu Val Pro Ser 20 25 30
 Ser Sar Ala Trp Lys Ser His Gly Ala Pro Ser Thr Arg Met Trr Ser 35 \hspace{1cm} 40 \hspace{1cm} 45
 Pro Gln Leu Leu Leu Ser Thr Arg Pro Pro Gln Ser Pro Ser Ala 50 55 60 ...
 Ser Pro Pro Ile Ala Arg Ala His Arg Thr His Pro His Phe Gly Asn
65 70 75 80
 Arg Leu Ser Ile Thr Cys Cys Asp Gly Arg Arg Ser Trp Arg Met Gly 85 90 95
Gln His Gly Pro Cys His Leu Asn Leu Gln Thr Thr His Pro Ala His 100 105 110
Ser Ser Glm Ala Leu Pro Ala Thr His Glm Pro Leu Gly Pro Trp Cys 115 120 125
Ser Ser Pro Ser Pro Phe Pro Ser Lys Leu Pro Ser Ala Gly Lou Arg
Pro Pro Ala Leu Gly Pro Trp Met Arg Arg Gly Pro Trp Pro Gln Ser 145
Trp Gln Met Gly Met His Pro Thr Val Gly Leu Xaa
165 170
<210> 215
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation
<400> 215
Met Trp Leu Leu Ile Ile Phe Cys Lys Ser Ala Ser Ala Ser Val Leu
1 5 10 15
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Cys Trp Ile Lys Lys Phe His Pro Val Phe Gln Glu Ser Leu Leu Tyr 20 25 30

Leu Val Gl<br/>n Glu Gly Ser Leu Cys Tyr Val Gl<br/>n Gl<br/>n Lys Val Pro Xaa 35 40 45

<210> 216

<211> 139 <212> PRT

<213> Homo sapiens

<400> 216

Met Glu Ala Val Val Phé Val Phe Ser Leu Leu Asp Cys Cys Ala Leu 1 5 10 15

Ile Phe Leu Ser Val Tyr Phe Ile Ile Thr Leu Ser Asp Leu Glu Cys 20 25 30

Asp Tyr Ile Asn Ala Arg Ser Cys Cys Ser Lys Leu Asn Lys Trp Val 35 40 45

Ile Pro Glu Leu Ile Gly His Thr Ile Val Thr Val Leu Leu Leu Met 50 60

Ser Leu His Trp Phe Ile Phe Leu Leu Asn Leu Pro Val Ala Thr Trp 65 70 75 80

Asn Ile Tyr Arg Tyr Ile Met Val Pro Ser Gly Asn Met Gly Val Phe 85 90 95

Asp Pro Thr Glu Ile His Asn Arg Gly Gln Leu Lys Ser His Met Lys 100 105 110

Glu Ala Met Ile Lys Leu Gly Phe His Leu Leu Cys Phe Phe Met Tyr 115 120 125

Leu Tyr Ser Met Ile Leu Ala Leu Ile Asn Asp 130 135

<210> 217

<211> 41

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Kaa equals stop translation

<400> 217

Met Ser Gly Ser Ser Leu Pro Ser Ala Leu Ala Leu Ser Leu Leu 1 5 10 15

```
Val Ser Gly Ser Leu Leu Pro Gly Pro Gly Ala Ala Gln Asn Val Arg 20 25 30 .
```

Val Gln Ser Cly Gln Asp Gln Lys Kaa

<210> 218

<211> 52

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (52)

<223> Xaa equals stop translation

<400> 218

Met Pro Ser His Ilc Arg Ala His Leu Phe Leu Leu Leu Phe Phe Leu 1 5 10 15

Phe Ile Tyr Gln Gly Ile Ser Ser Ile Ser Gln Ala Ser Gly Leu Thr 20 25 30

Leu Lys Thr Gln Asn Glu Lys Asp Ile Gln Val Ser Ile Leu Lys Glu 35 40 45

Phe Val Val Xaa 50

<210> 219

<211> 49 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (19)

<223> Xaa equals stop translation

<400> 219

Met Cys Ile Tyr Gln Ser Glu Gln Met Leu Ala Leu Leu Leu Val Leu

Val Phe Cys Ile Ser Leu Leu Val Leu Val Cys Trp Gly Ser His Asn 25

Lys Val Pro Gln Lys Phe Ile Phe Ser Gln Phe Trp Gly Leu Glu Asp  $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$ 

Xaa

<210> 220

<211> 42 <212> PRT

<213> Homo sapiens

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<220>
 <221> SITE
 <222> (42)
 <223> Xaa equals stop translation
 <400> 220
 Met Ala Val Pro Leu Phe Leu Tyr Ile Phe Thr Leu Leu Pro Leu Leu
 Pro Phe Leu Leu Ser Leu Cys Phe Ser Pro Leu Thr Val Lys Arg Ser 20 25 30
 Ser Ser Ser Clu Ser Lys Ser Ser Leu Xaa
<210> 221 - <211> 41
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation
<400> 221
Met Cly Met Leu Leu Ala Phe Trp Leu Pro Gly Ala Ser Trp Gln Glu

1 5 10 25
Ala Gly Pro Arg Ala Ser Thr Gln Arg Met Arg Thr Gln Thr Gln Met 20 \phantom{-}25\phantom{+} 30
Ser Thr Arg Lys ≥ro Lys Pro Ala Xaa
35 40
<210> 222
<211> 43
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (43)
<223> Xaa equals stop translation
<400> 222
Met Glu Pro Ala Met Val Leu Lys Phe Leu Ser Ser Leu Pro Glu Asn
Leu Phe Leu Pro Ser Leu Leu Phe Phe Ala Trp Leu Cys Trp Asn Met 20 25 30
Val Cys Gly Ser Pro Val Ser Cys Pro Tyr Xaa
35 40 .
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<210> 223
<211> 204
<212> PRT
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<213> Homo sapiens

<220>

<221> SITE

<222> (204)

<223> Xaa equals stop translation

Met Gln Leu Gly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly Cys

1 10 15

Phe Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg Lys 20 25 30

Pro Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala Val 35 40 45

Leu Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe Ala 50 . 55 60

Leu Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr Ile 65 70 75 80

Gly Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr Ser 85 90 95

Arg Thr Val Ala Ile Ile Gly Gly Phe Leu Val Leu Ala Ser Gly Ala 100  $\phantom{\bigg|}$  105  $\phantom{\bigg|}$  110

Gly Glu Leu Tyr Arg Arg Lys Pro Arg Ser Arg Ser Leu Gln Ser Thr 115 120 125

Gly Gln Val Phe Leu Gly Ile Tyr Leu Ile Cys Val Ala Tyr Ser Leu 130 135 140

Gln His Ser Lys Gl: Asp Arg Leu Ala Tyr Leu Asn His Leu Pro Gly 145 150 150 160

Gly Glu Leu Met Ile Gln Leu Phe Phe Val Leu Tyr Gly Ile Leu Ala 165 170 175

Pro Gly Leu Ser Val Arg Leu Leu Arg Asp Pro Arg Cys Pro Asp Pro 180 185 . 190

Gly Cys Thr Ala Ala Pro Cys His Ala Ala His Xaa

<210> 224

<211> 43

<212> PRT

<213> Homo sapiens

<221> SITE <222> (43)

WO 00/06698 PCT/US99/17130

160

<223> Xaa equals stop translation

Met Arg Val Arg Ile Gly Leu Thr Leu Leu Leu Cys Ala Val Leu Leu

1 5 10 15

Ser Leu Ala Ser Ala Ser Ser Asp Glu Glu Glu Ser Gln Asp Glu Ser 20 25 30

Leu Gly Phe Gln Asp Tyr Phe Asp Ile Arg Xaa 35

<210> 225

<211> 156

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (156)

<223> Xaa equals stop translation

<400> 225

Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly

1 5 10 15

Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu GIn Ala Pro Gly 20 25 30

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Cys Met Asp Cys Ser Thr Ser Cys Pro Leu Pro Ala Ala Leu Ala His 50 55 60

Pro Trp Gly Arg Ser Glu Pro Asp Leu Arg Ala Gly Ala Ala Phe Trp 65 .70 .75 80

Leu Phe Gly Leu Glu Thr Met Pro Gln Glu Arg Glu Val His His Pro 85 90 95

His Arg Gly Asp Arg Arg Gly Leu Pro Ser Cys Gly Ala Asp Pro 100 105 110

Val Thr Ket Cys Pro Leu Pro Ala Gly Ala Arg Pro Leu Ile Ile His

Ser Ser Ile Leu Glu Pro Val Ser Ala Ser Gln Thr Arg Arg Glu Pro 135

Ser Ser Ser Asn His Lys Gly Gly Gly Gly Arg Xaa 145 150 155

<210> 226

<211> 74 <212> PRT

<213> Homo sapiens

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<220>
 <221> SITE
 <222> (38)
 <223> Xaa equals any of the naturally occurring L-amino acids
 <221> SITE
 <222> (48)
 <223> Xaa equals any of the naturally occurring L-amino acids
 <220>
 <221> SITE
 <222> (54)
 <223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (55)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (74)
<223> Xaa equals stop translation
<400> 226
Met. Phe Tyr Lys Leu Thr Leu Ile Leu Cys Glu Leu Ser Val Ala Gly
1 5 10 15
Val Thr Gln Ala Ala Ser Gln Arg Pro Leu Gln Arg Leu Pro Arg His 20 25 30
Ile Cys Ser Gln Arg Kaa Pro Pro Gly Arg Cys Leu Leu Lys Ala Kaa
                               40
Leu Gln Thr Thr Trp Kaa Xaa Pro Asp Lys Pro Ile Pro Arg Leu Ser
                          55
Pro Pro Leu Xaa Ser Asp Pro Lys Arg Xaa
65 70
<210> 227
<211> 167
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (167)
<223> Xaa equals stop translation
<400> 227
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Met Gly Ser Arg Phe Leu Leu Val Leu Leu Ser Gly Leu Thr Val Leu  $\frac{1}{1}$ .

Leu Ala Leu Pro Gly Ser Glu Ala Lys Asn Ser Gly Ala Ser Cys Pro 20 25 30

Pro Cys Pro Lys Tyr Ala Ser Cys His Asr. Ser Thr His Cys Thr Cys  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Glu Asp Gly Phe Arg Ala Arg Ser Gly Arg Thr Tyr Phe His Asp Ser 50 55 60

Ser Glu Lys Cys Glu Asp Ile Asn Glu Cys Glu Thr Gly Leu Ala Lys 65 70 75 80

Cys Lys Tyr Lys Ala Tyr Cys Arg Asn Lys Val Gly Gly Tyr Ile Cys 85  $_{\odot}$  90 95

Scr Cys Leu Val Lys Tyr Thr Leu Phe Asn Phe Leu Ala Gly Ile Ile

Asp Tyr Asp His Pro Asp Cys Tyr Glu Asn Asn Ser Gln Gly Thr Thr 115 120 125

Gln Ser Asn Val Asp Ile Trp Val Ser Gly Val Lys Pro Gly Phe Gly 130 135 140

Lys Gln Leu Val Arg Ile Thr Met Pro Phe Ser Tyr Pro Asn Ile Asn 150 155 160

Met Ser Ser Cys Asp Phe Xaa 165

<210> 228 <211> 71

<212> PRT

<213> Homo sapiens

<221> SITE

<222> (71)

<223> Xaa equals stop translation

Met Lys Pro Lys His Leu Glu Trp Cys Leu Ala His Ser Trp Cys Val 1 5 10 15

Ile Trp Leu Ser Phe Val Ser Pro Pro Thr Ser His Leu Glu Cys Asp
20 25 30

Gly Phe Pro Gly Ser Leu Leu Pro Pro Cys Glu Glu Gly Arg Cys Phe 35 40 45

Pro Phe Thr Phe His His His Asp Cys His Gly Cys Ser Pro Leu Gln 50 55 60

Ser Ser Pro Gly Gln His Xaa 70

<210> 229 <211> 273 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (273) <223> Xaa equals stop translation <400> 229 Met Cys Cys Trp Pro Leu Leu Leu Trp Gly Leu Leu Pro Gly Thr 1 5 10 Ala Ala Gly Gly Ser Gly Arg Thr Tyr Pro His Arg Thr Leu Leu Asp  $20 \ \ 25 \ \ \ 30$ Ser Glu Gly Lys Tyr Trp Leu Gly Trp Ser Gln Arg Gly Ser Gln Ile  $^{35}$  40 45 Ala Phe Arg Leu Cln Val Arg Thr Ala Cly Tyr Val Gly Phe Gly Phe 50 55 60 Ser Pro Thr Gly Ala Met Ala Ser Ala Asp Ile Val Val Gly Gly Val 65 70 75 80 Ala His Gly Arg Pro Tyr Leu Gln Asp Tyr Phe Thr Asn Ala Asn Arg 85. 90 95 Glu Leu Lys Lys Asp Ala Gln Gln Asp Tyr His Leu Glu Tyr Ala Met 100 105 110 Glu Asn Ser Thr His Thr Ile Ile Glu Phe Thr Arg Glu Leu His Thr 115 120 125 Cys Asp Ile Asn Asp Lys Ser Ile Thr Asp Ser Thr Val Arg Val Ile 130 \$135\$Trp Ala Tyr His His Glu Asp Ala Gly Glu Ala Gly Pro Lys Tyr His 145 150 155 160Asp Scr Asn Arg Gly Thr Lys Scr Leu Arg Leu Leu Asn Pro Glu Lys 165  $170^{\circ}$ . Thr Scr Val Leu Ser Thr Ala Leu Pro Tyr Phe Asp Leu Val Asm Glm 180 185 199 Asp Val Pro Ile Pro Asn Lys Asp Thr Thr Tyr Trp Cys Gln Met Phe 195 200 205 Lys Ile Pro Val Phe Gln Glu Lys His His Val Ile Lys Val Glu Pro 210 215 220 Val Ile Gln Arg Gly His Glu Ser Leu Val His His The Leu Leu Tyr 225 230 235 240 Gln Cys Ser Asn Asn Phe Asn Asp Ser Val Fro Gly 1le Arg Ala Arg

245 250 Ile Ala Ile Thr Pro Thr Cys Pro Met His Ser Ser Pro Val Lys Leu 260 265 270 Xaa <210> 230 <211> 82 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (82) <223> Xaa equals stop translation <400> 230 Met Arg Pro Gly Thr Ala Leu Gln Ala Val Leu Leu Ala Val Leu Leu 1 5 10 15 Val Gly Leu Arg Ala Ala Thr Gly Arg Leu Ser Gly Gln Pro Val  $20 \hspace{1cm} 25 \hspace{1cm} 30$ Cys Arg Gly Gly Thr Gln Arg Pro Cys Tyr Lys Val Ile Tyr Phe His Asp Thr Ser Arg Arg Leu Asn Phe Glu Glu Ala Lys Glu Ala Cys Arg 50  $\phantom{0}$  55  $\phantom{0}$  60 Arg Gly Trp Arg Pro Ala Ser Gln His Arg Val Leu Lys Met  $\Lambda$ sn Arg 65  $\cdot$  70  $\cdot$  75 80 Asn Xaa

<210> 231

<211> 71

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (38)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 231

<400> 231
Met Ser Pro Leu Ser Ala Ala Arg Ala Ala Leu Arg Val Tyr Ala Val
5
10
15

Gly Ala Ala Val Ile Leu Ala Gln Leu Leu Arg Arg Cys Arg Gly Gly 20 25 30

Phe Leu Glu Pro Val Kaa Pro Pro Arg Pro Asp Arg Val Ala Ile Val 35

Thr Gly Gly Thr Asp Gly Ile Gly Tyr Ser Thr Ala Asn Ile Trp Arg
50 55 60

Asp Leu Ala Cys Met Leu Ser 65 70

<210> 232

<211> 225

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (5)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 232

His Glu Arg Ala Xaa Gly Pro Ser Arg Gly His Gly Glu Leu Leu Ser 1 5 10 15

Cys Val Leu Gly Pro Arg Leu Tyr Lys Ile Tyr Arg Glu Arg Asp Ser 20 25 30

Glu Arg Ala Pro Ala Ser Val Pro Glu Thr Pro Thr Ala Val Thr Ala 35 40 45

Pro His Ser Ser Ser Trp Asp Thr Tyr Tyr Gln Pro Arg Ala Leu Glu 50 60

Lys His Ala Asp Ser Ile Leu Ala Leu Ala Ser Val Phe Trp Ser Ile 65 70 75 80

Ser Tyr Tyr Ser Ser Pro Phe Ala Phe Phe Tyr Leu Tyr Arg Lys Gly 85 90 95

Tyr Leu Ser Leu Ser Lys Val Val Pro Phe Ser His Tyr Ala Gly Thr 100 105 110

Leu Leu Leu Leu Ala Gly Val Ala Cys Ser Glu Ala Leu Ala Ala 115 . 120 . 125

Gly Pro Thr Pro Ser Thr Gly Ser Ser Ser Pro Ser Trp Lys Gln His 130 135 140

Ile Gly Thr Ser Leu Gln Lys Thr Arg Gly Ser Leu Pro Thr Thr Thr 145 150 155 160

Leu Thr Ser Gly Ala Gly Gln Ser Thr Ser Thr Gly Lys Asn Pro Ala 165 170 175

Ala Gly Arg Scr Leu Glu Gly Ala Leu Pro Ala Gly Val Trp Pro Cys 180 185 190

Phe Ala Gln Ser Pro Cys Thr Gly Gly Gln Gln Thr Pro Ser Ser Thr 195 200 205

Gly Leu Arg Ser Cys Leu Val Arg Ser Pro Ala Thr Trp Trp Arg Thr 210 215 220

Pro 225 <210> 233 <211> 314 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (147) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (211) <223> Xaa equals any of the naturally occurring L-amino acids <400> 233 Met Leu Pro Ala Arg Lou Pro Phe Arg Leu Leu Ser Leu Phe Leu Arg 1 5 10 15 Gly Ser Ala Pro Thr Ala Ala Arg His Gly Leu Arg Glu Pro Leu Leu 20 25 30Glu Arg Arg Cys Ala Ala Ala Ser Ser Phe Gln His Ser Ser Leu 35 40 45 Gly Arg Glu Leu Pro Tyr Asp Pro Val Asp Thr Glu Gly Phe Gly Glu 50 55 60 Gly Gly Asp Met Gln Glu Arg Phe Leu Phe Pro Glu Tyr Ile Leu Asp 65 70 75 80 Pro Glu Pro Gln Pro Thr Arg Glu Lys Gln Leu Gln Glu Leu Gln Gln 61 85 90 95 Gln Gln Glu Glu Glu Arg Gln Arg Gln Gln Arg Arg Glu Glu Arg 100 105 110Arg Gln Gln Asn Leu Arg Ala Arg Ser Arg Glu His Pro Val Val Gly His Pro Asp Pro Ala Leu Pro Pro Ser Gly Val Asn Cys Ser Gly Cys 130 135 140 Gly Ala Xaa Leu His Cys Gln Asp Ala Gly Val Pro Gly Tyr Leu Pro 145 150 155 160 Arg Glu Lys Phe Leu Arg Thr Ala Glu Ala Asp Gly Gly Leu Ala Arg 165 170 175 Thr Val Cys Gln Arg Cys Trp Leu Leu Ser His His Arg Arg Ala Leu 180 185 190 Arg Leu Gln Val Ser Arg Glu Gln Tyr Leu Glu Leu Val Ser Ala Ala 195 200 205 .

Leu Arg Xaa Pro Gly Pro Ser Leu Val Leu Tyr Met Val Asp Leu Leu 210 215 220

Asp Leu Pro Asp Ala Leu Leu Pro Asp Leu Pro Ala Leu Val Gly Pro 225 230 235 240

Lys Gln Leu Ile Val Leu Gly Asn Lys Val Asp Leu Leu Pro Gln Asp 245 250 255

Ala Pro Gly Tyr Arg Gln Arg Leu Arg Glu Arg Leu Trp Glu Asp Cys 260 265 270

Ala Arg Ala Gly Leu Leu Leu Ala Pro Gly Thr Lys Gly His Ser Ala 275 280 285

Pro Ser Arg Thr Ser His Arg Thr Gly Arg Ile Arg Ile Arg Thr 290  $\phantom{-}295\phantom{+}\phantom{0}$ 

Gly Pro Ala Gln Trp Ser Gly Thr Cys Gly 305

<210> 234 <211> 93

<212> PRT

<213> Homo sapiens

Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu Arg Gly Leu 1 5 10 15

Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser Ala Ser Glu 20 25 30

Ile Pro Lys Gly Lys Gln Lys Ala His Ser Gly Arg Gly Arg Trp Trp 35 40 .

Thr Cys Ile Met Glu Cys Ala Tyr Lys Gly Gln Gln Glu Cys Leu Val 50 60

Glu Thr Gly Ala Leu Gly Pro Met Ala Phe Arg Val His Leu Gly Ser 65 70 75 80

Gln Val Gly Met Asp Ser Lys Glu Lys Arg Gly Asn Val 85 90

<210> 235

<211> 73 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (73)

<223> Xaa equals stop translation

<400> 235

168

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Met Gly Ser Ala Ala Leu Glu Ile Leu Gly Leu Val Leu Cys Leu Val
 Gly Trp Cly Cly Leu Ile Leu Ala Cys Gly Leu Pro Met Trp Gln Val
Thr Ala Phe Leu Asp His Asn Ile Val Thr Ala Cln Thr Thr Trp Lys
Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly Thr Cys Ser Ala
Lys Cys Thr Thr Arg Cys Trp Leu Xaa
                      70
<210> 236
<211> 349
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (283)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (293)
<223> Xaa equals any of the naturally occurring L-amino acids
<221> SITE
<222> (325)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (326)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (349)
<223> Xaa equals stop translation
<400> 236
Met Leu Cys Pro Trp Arg Thr Ala Asn Leu Gly Leu Leu Leu Ile Leu
1 5 10 15
Thr Ile Phe Leu Val Ala Glu Ala Glu Gly Ala Ala Gln Pro Asn Asn
Ser Leu Met Leu Gln Thr Ser Lys Glu Asn His Ala Leu Ala Ser Ser
Ser Leu Cys Met Asp Glu Lys Gln Ile Thr Gln Asn Tyr Ser Lys Val
```

Leu	Ala	Giu	Val	Asn	Thr	Ser	Trp	Pro	Val	Lvs	Met.	Ala	Thr.	Asn	A1=
65					70		•			75			••••		. 80

- Val Leu Cys Cys Pro Pro Ile Ala Leu Arg Asn Leu Ile Ile Ihr 85 90 95
- Trp Glu Ile Ile Leu Arg Gly Glr Pro Ser Cys Thr Lys Ala Tyr Lys 100 105 110
- Lys Glu Thr Asn Glu Thr Lys Glu Thr Asn Cys Thr Asp Glu Arg Ile 115 120 125
- Thr Trp Val Ser Arg Pro Asp Gln Asn Ser Asp Leu Gln Ile Arg Thr 130 135 140
- Val Ala Ile Thr His Asp Gly Tyr Tyr Arg Cys Ile Met Val Thr Pro 145 150 150 160
- Asp Gly Asn Phe His krg Gly Tyr His Leu Gln Val Leu Val Thr Pro 165 170 175
- Glu Val Thr Leu Phe Gln Asn Arg Asn Arg Thr Ala Val Cys Lys Ala 180 185 190
- Val Ala Gly Lys Pro Ala Ala His Ile Ser Trp Ile Pro Glu Gly Asp 195 200 205
- Cys Ala Thr Lys Cln Glu Tyr Trp Ser Asn Gly Thr Val Thr Val Lys 210 215 220
- Ser Thr Cys His Trp Glu Val His Asn Val Ser Thr Val Asn Cys His 225 230 235 240
- Val Ser His Leu Thr Gly Asn Lys Ser Leu Tyr Ile Glu Leu Leu Pro 245 250 255
- Val Pro Gly Ala Lys Lys Ser Ser Lys Leu Tyr Ile Pro Tyr Ile Ile 260 265 270
- Leu Thr Ile Ile Ile Leu Thr Ile Val Gly Xaa Ile Trp Leu Leu Lys 275 280 285
- Val Asn Gly Cys Xaa Lys Tyr Lys Leu Asn Lys Pro Glu Ser Thr Pro 290 295 300
- Val Val Glu Glu Asp Glu Met Gln Pro Tyr Ala Phe Tyr Thr Glu Lys 305 310 315 320
- Asn Asn Pro Leu Xaa Xaa Thr Thr Asn Lys Val Lys Ala Ser Glu Ala 325 330 335
- Leu Gln Ser Glu Val Asp Thr Asp Leu His Thr Leu Xaa  $340 \hspace{1.5cm} 345$

<210> 237

<211> 17

<212> PRT

<213> Homo sapiens

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<400> 237
Leu Ala Leu Tyr Ser Ala Leu Phe Ser Tyr Ser Gly Trp Asp Thr Leu
                                          10
Asn
<210> 238
<211> 14
<212> PRT
<213> Homo sapiens
<400> 238
Val Thr Glu Glu Ile Lys Asn Pro Glu Arg Asn Leu Pro Leu

1 5 10
               5
<210> 239
<211> 9
<212> PRT
<213> Homo sapiens
<400> 239
Ile Gly Ile Ser Met Pro Ile Val Thr
<210> 240
<211> 13
<212> PRT
<213> Homo sapiens
<400> 240
Ile Tyr Ile Leu Thr Asn Val Ala Tyr Tyr Thr Val Leu
<210> 241
<211> 11
<212> PRT
<213> Homo sapiens
<400> 241
Ser Asp Ala Val Ala Val Thr Phe Ala Asp Gln 1 5 10
<210> 242
<211> 13
<212> PRT
<213> Eomo sapiens
<400> 242
Val Ala Leu Ser Cys Phe Gly Gly Leu Asn Ala Ser Ile
```

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<210> 243
<211> 15
<212> PRT
<213> Homo sapiens
<400> 243
Ser Arg Leu Phe Phe Val Gly Ser Arg Glu Gly His Leu Pro Asp
1 5 10
<210> 244
<211> 11
<212> PRT
<213> Homo sapiens
<400> 244
Ser Phe Ser Tyr Trp Phe Phe Val Cly Leu Ser
<210> 245 .
<211> 11
<212> PRT
<213> Homo sapiens
<400> 245
Val Gly Gln Leu Tyr Leu Arg Trp Lys Glu Pro
1 5 10
<210> 246
<211> 16
<212> PRT
<213> Homo sapiens
<400> 246
<210> 247
<211> 9
<212> PRT
<213> Homo sapiens
<400> 247
Asp Thr Ile Asm Ser Leu Ile Gly Ile
<210> 248
<211> 44
<212> PRT
<213> Homo sapiens
<400> 248
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Ala Thr Ala Leu Pro Pro Lys Ile Val Gly Ser Ala Thr Arg Tyr Leu  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15 \hspace{1.5cm} \cdot$ 

Gln Val Leu Cys Met Ser Val Ala Ala Glu Met Asp Leu Glu Asp Gly 20 25 30

Gly Glu Met Pro Lys Gln Arg Asp Pro Lys Ser Asn 35

<210> 249

<211> 352

<212> PRT

<213> Homo sapiens

<400> 249

Leu Leu Ala Ala Ala Cys Ile Cys Leu Leu Thr Phe Ile Asn Cys Ala 1 5 10 15

Tyr Val Lys Trp Gly Thr Leu Val Gln Asp Ile Phe Thr Tyr Ala Lys  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Val Leu Ala Leu Ile Ala Val Ile Val Ala Gly Ile Val Arg Leu Gly 35 . 40 45

Gln Gly Ala Ser Thr His Phe Glu Asn Ser Phe Glu Gly Ser Ser Phe
50 55 60

Ala Val Gly Asp Ile Ala Leu Ala Leu Tyr Ser Ala Leu Phe Ser Tyr 65 70 75 80

Ser Gly Trp Asp Thr Leu Asn Tyr Val Thr Glu Glu Ile Lys Asn Pro 85 90 95

The lie Tyr Ile Leu Thr Asn Val Ala Tyr Tyr Thr Val Leu Asp Met 115 120 125

Arg Asp Ile Leu Ala Ser Asp Ala Val Ala Val Thr Phe Ala Asp Gln 130 135 140

Ile Phe Gly Ile Phe Asn Trp Ile Ile Pro Leu Ser Val Ala Leu Ser 145 150 155 160

Cys Phe Gly Gly Leu Asn Ala Ser Ile Val Ala Ala Ser Arg Leu Phe 165 170 175

Phe Val Gly Ser Arg Glu Gly His Leu Pro Asp Ala Ile Cys Met Ile 180 185 190

His Val Glu Arg Phe Thr Pro Val Pro Ser Leu Leu Phe Asn Gly Ile 195 200 205

Net Ala Leu Ile Tyr Leu Cys Val Glu Asp Ile Phe Gln Leu Ile Asn 210 215 220

Tyr Tyr Ser Phe Ser Tyr Trp Phe Phe Val Gly Leu Ser Ile Val Gly

WO 00/06698 PCT/US99/17130

173

225 230 Gln Leu Tyr Leu Arg Trp Lys Glu Pro Asp Arg Pro Arg Pro Leu Lys 245 250 255 Leu Ser Val Phe Phe Pro Ile Val Phe Cys Leu Cys Thr Ile Phe Leu 260 265 270 Val Ala Val Pro Leu Tyr Ser Asp Thr Ile Asn Ser Leu Ile Gly Ile 275 280 285 Ala Ile Ala Leu Ser Gly Leu Pro Phe Tyr Phe Leu Ile Ile Arg Val 290 295 300 Pro Glu His Lys Arg Pro Leu Tyr Leu Arg Arg Ile Val Gly Ser Ala  $^\circ$  305 310 315 320 Thr Arg Tyr Leu Gln Val Leu Cys Met Ser Val Ala Ala Glu Met Asp 325 330 335 Leu Glu Asp Gly Glu Met Pro Lys Gln Arg Asp Pro Lys Ser Asn 340 345 350

<210> 250 <211> 119 <212> PRT

<213> Homo sapiens

<400> 250

Ala Ala Arg Gly Ser Gly Val Arg Asp Pro Leu Glu Glu Ala Val Cys 1 5 10 15

Pro Phe Ser Asp Leu Gln Leu His Ala Gly Arg Thr Thr Ala Leu Phe 20 25 30

Lys Ala Val Arg Gln Gly His Leu Ser Leu Gln Arg Leu Leu Ser  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Phe Val Cys Leu Cys Pro Ala Pro Arg Gly Gly Ala Tyr Arg Gly Arg 50 55 60

Gln Ala Ser Leu Ser Cys Gly Gly Leu His Pro Val Arg Ala Ser Arg 65 70 75 ... 80

Leu Leu Cys Leu Pro Lys Gln Ala Trp Ala Met Ala Gly Ala Pro Pro 85 90 95

Pro Val Ser Leu Pro Pro Cys Ser Leu Ile Ser Asp Cys Cys Ala Ser 100 105 110

Asn Gln Arg Asp Ser Val Gly 115

<210> 251

<211> 356 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (37) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE <222> (280) <223> Xaa equals any of the naturally occurring L-amino acids Leu Ser Lys Ala Phe Leu Asp Ser Pro Asn Arg Leu Leu Ala Val Glu 1 5 10 15 Met Asn Thr Asp His Leu Arg Leu Thr Val Pro Asn Gly IIe Gly Ala 20 25 30Leu Lys Leu Arg Kaa Met Glu His Tyr Phe Ser Gln Gly Leu Ser Val Gln Leu Phe Asn Asp Gly Ser Lys Gly Lys Leu Asn His Leu Cys Gly 50 55 60 Ala Asp Phe Val Lys Ser His Gln Lys Pro Pro Gln Gly Met Glu Ile 65 70 75 80 Lys Ser Asn Glu Arg Cys Cys Ser Phe Asp Gly Asp Ala Asp Arg Ile 85 90 95 . Val Tyr Tyr Tyr His Asp Ala Asp Gly His Phe His Leu Ile Asp Gly 100 105 110 Asp Lys Ile Ala Thr Leu Ile Ser Ser Phe Leu Lys Glu Leu Leu Val 115 120 125 Glu Ile Gly Glu Ser Leu Asn Ile Gly Val Val Gln Thr Ala Tyr Ala 130 135 140 Asn Gly Ser Ser Thr Arg Tyr Leu Glu Glu Val Met Lys Val Pro Val 145 Tyr Cys Thr Lys Thr Gly Val Lys His Leu His His Lys Ala Cln Glu 165 170 175 Phe Asp Ile Gly Val Tyr Phe Glu Ala Asn Gly His Gly Thr Ala Leu 180 185 190 Phe Ser Thr Ala Val Clu Mct Lys Ile Lys Gln Ser Ala Glu Gln Leu 195 200 205 Glu Asp Lys Lys Arg Lys Ala Ala Lys Met Leu Glu Asn Ile Ile Asp 210 215 220 Leu Phe Asn Gln Ala Ala Gly Asp Ala Ile Ser Asp Met Leu Val Ile

230

235

Glu Ala Ile Leu Ala Leu Lys Gly Leu Thr Val Gln Gln Trp Asp Ala 245  $\phantom{\bigg|}250\phantom{\bigg|}$  250  $\phantom{\bigg|}25\phantom{\bigg|}$ 

Leu Tyr Thr Asp Leu Pro Asn Arg Gln Leu Lys Val Gin Val Ala Asp 260 265 270

Arg Arg Val Ile Ser Thr Thr Xaa Ala Glu Arg Gln Ala Val Thr Pro 275 280 285

Pro Gly Leu Gln Glu Ala Ile Asn Asp Leu Val Lys Lys Tyr Lys Leu 290 295 300

Ser Arg Ala Phe Val Arg Pro Ser Gly Thr Glu Asp Val Val Arg Val 310 315 320

Tyr Ala Glu Ala Asp Ser Gln Glu Ser Aia Asp His Leu Ala His Glu 325 330 335

Val Ser Leu Ala Val Phe Gln Leu Ala Gly Gly Ile Gly Glu Arg Pro  $340 \hspace{1cm} 345 \hspace{1cm} 350$ 

Gln Pro Gly Phe 355

<210> 252

<211> 26

<212> PRT

<213> Homo sapiens

<400> 252

Leu Ser Lys Ala Phc Leu Asp Ser Pro Asn Arç Leu Leu Ala Val Glu 1 5 10 15

Met Asn Thr Asp His Leu Arg Leu Thr Val 20 25

<210> 253

<211> 28

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (11)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 253

Pro Asn Gly Ile Gly Ala Leu Lys Leu Arg Xaa Met Glu His Tyr Phe
1 5 10 15

Ser Gln Gly Leu Ser Val Gln Leu Phe Asn Asp Gly 20 25

<210> 254

<211> 28

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<212> PRT
 <213> Homo sapiens
 <400> 254
 Ser Lys Gly Lys Leu Asn His Leu Cys Gly Ala Asp Phe Val Lys Ser
1 5 10 15
 His Gln Lys Pro Pro Gln Gly Met Glu Ile Lys Ser
 <210> 255
 <211> 28
 <212> PRT
 <213> Homo sapiens
 <400> 255
Asn Glu Arg Cys Cys Ser Phe Asp Gly Asp Ala Asp Arg Ile Val Tyr

1 5 10 15
Tyr Tyr His Asp Ala Asp Gly His Phe His Leu Ile 20 \\ 25
<210> 256
<211> 28
<212> PRT
<213> Homo sapiens
<400> 256
Asp Gly Asp Lys Ile Ala Thr Leu Ile Ser Ser Phe Leu Lys Glu Leu
1 5 10 15
Leu Val Glu Ile Gly Glu Ser Leu Asn Ile Gly Val
<210> 257
<211> 28
<212> PRT
<213> Homo sapiens
<400> 257
Val Gln Thr Ala Tyr Ala Asn Gly Ser Ser Thr Arg Tyr Leu Glu Glu 1 5 10 15
Val Met Lys Val Pro Val Tyr Cys Thr Lys Thr Gly
<210> 258
<211> 28
<212> PRT
<213> Homo sapiens
<400> 258
Val Lys His Leu His His Lys Ala Gln Glu Phe Asp Ile Gly Val Tyr

1 5 10 15
```

```
Phe Glu Ala Asn Gly His Gly Thr Ala Leu Phe Ser 20 . 25
 <210> 259
 <211> 28
 <212> PRT
 <213> Homo sapiens
 <400> 259
Thr Ala Val Glu Met Lys Ile Lys Gln Ser Ala Glu Gln Leu Glu Asp
1 5 10 15
Lys Lys Arg Lys Ala Ala Lys Met Leu.
Glu As<br/>n Ile 20 \\ \hspace{1.5cm} 25
<210> 260
<211> 28
<212> PRT
<213> Homo sapiens
<400> 260
Val Ile Glu Ala Ile Leu Ala Leu Lys Gly Leu Thr $20\ 25
<210> 261
<211> 28
<212> PRT
<213> Homo sapiens
<400> 261
Val Gln Gln Trp Asp Ala Leu Tyr Thr Asp Leu Pro Asn Arg Gln Leu
Lys Val Gln Val Ala Asp Arg Arg Val Ile Ser Thr
<210> 262
<211> 28
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (2)
<223> Kaa equals any of the naturally occurring L-amino acids
<400> 262
Thr Xaa Ala Glu Arg Gln Ala Val Thr Pro Pro Gly Leu Gln Glu Ala
Tle Asn'Asp Leu Val Lys Lys Tyr Lys Leu Ser Arg
```

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<210> 263
 <211> 24
 <212> PRT
 <213> Homo sapiens
 <400> 263
Ala Phe Val Arg Pro Ser Gly Thr Glu Asp Val Val Arg Val Tyr Ala
1 5 10 15
Glu Ala Asp Ser Gln Glu Ser Ala
             20
<210> 264
<211> 26
<212> PRT
<213> Homo sapiens
<400> 264
Asp His Leu Ala His Glu Val Ser Leu Ala Val Phe Gln Leu Ala Gly
Gly Ile Gly Glu Arg Pro Gln Pro Gly Phe
<210> 265
<211> 443
<212> PRT
<213> Homo sapiens
<400> 265
Gly Thr Arg Ala Ala Pro Gly Leu Gly Ala Trp Gly Arg Arg Ser Pro
1 5 10 15
Pro Ser Phe Ser Pro Pro Arg Pro Arg Pro Gly Val Met Ala Gly 20 25 30
Leu Asn Cys Gly Val Ser Ile Ala Leu Leu Gly Val Leu Leu Gly 35 \hspace{1cm} 45
Ala Ala Arg Leu Pro Arg Gly Ala Glu Ala Phe Glu Ile Ala Leu Pro 50 \hspace{1cm} 55 \hspace{1cm} 60
Arg Glu Ser Asn Ile Thr Val Leu Ile Lys Leu Gly Thr Pro Thr Leu 65 70 75 80
Leu Ala Lys Pro Cys Tyr Ile Val Ile Ser Lys Arg His Ile Thr Met
Leu Ser Ile Lys Ser Gly Glu Arg Ile Val Phe Thr Phe Ser Cys Gln
100 105 110
                                   105
Ser Pro Glu Asn His Phe Val Ile Glu Ile Gln Lys Asn Ile Asp Cys
115 120 125
```

Net Ser Gly Pro Cys Pro Phe Gly Glu Val Gln Leu Gln Pro Ser Thr

	13	U				13	5				140	)			
Se:	Le	u Le	u Pr	o Th	r Le 15	u Ası O	n Ar	g Thi	Phe	11e	ттр	Asp	yal	Lys	Ala 160
His	Ly:	s Se	r Il	e Gl 16	y Le: 5	u Glu	ı Le	u Gln	170	e Ser	Tle	Pro	Arg	Leu 175	
Gln	Ile	e Gl	7 Pr	o G1 0	y <sub>.</sub> Gli	u Sei	г Су:	s Pro 185	Asp	Gly	Val	Thr	His 190		Ile
Ser	G13	/ Arg	ı Ile	e As	p Ala	a Thr	Va:	l Val	Arg	Ile	Gly	Thr 205		Суз	Ser
Asn	G1 <sub>3</sub> 210	Thi	va:	l Se	r Arç	215	Lys	s Met	Gln	Glu	Gly 220	Val	Lys	Met	Ala
Leu 225	His	Leu	ı Pro	Tr <sub>i</sub>	230	His	Pro	Arg	Asn	Val 235	Ser	Gly	Phe	Ser	lle 240
Ala	Asn	Arg	Ser	Ser 245	r Ile	. Lys	Arg	, Leu	Cys 250	Ile	Ile	Glu	Ser	Val 255	Phe
31u	Gly	Glu	Gly 260	Ser	Ala	Thr	Leu	Met 265	Ser	Ala	Asn	Tyr	Pro 270	Glu	Gly
		2/5					280					285			
Jeu	Arg 290	Ala	Ser	· Val	Ser	Phe 295	Leu	Asn	Phe	Asn	Leu 300	Ser	Asn	Cys	Glu
lrg 105	Lуз	Glu	Glu	Arg	Val 310	Glu	туг	Туг	Ile	Pro 315	Gly	Ser	Thr	Thr	Asn 320
				325				Lys	330					335	
			340					Cys 345					350		
		222					360	Val				365			
	370					375		Asp			380				
er 85	Leu	Thr	Ile	Glu	Pro 390	Arg	Pro	Val	Lys	Gln 395	Ser .	Arg	Lys		Val 400
ro	Gly	Cys	Phe	Val 405	Cys	Leu	Glu	Ser	Arg 410	Thr :	Cys :	Scr		Asn 415	Leu
hr	Leu	Thr	Ser 420	Gly	Ser	Lys	His	Lys 425	Ile	Ser	Phe I		Cys / 430	Asp.	Asp
еп	Thr	Arg 435	Leu	Trp	Met	Asn	Val 440	Glu i	Lys	Pro					

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<210> 266
 <211> 159
 <212> PRT
 <213> Homo sapiens
 <400> 266
 Phe Glu Ile Ala Leu Pro Arg Glu Ser Asn Ile Thr Val Leu Ile Lys
1 5 10 15
Leu Gly Thr Pro Thr Leu Leu Ala Lys Pro Cys Tyr Ile Val Ile Ser
20 25 30
Lys Arg His Ile Thr Met Leu Ser Ile Lys Ser Gly Glu Arg Ile Val 35 \ 40 \ 45
Phe Thr Phe Ser Cys Gln Ser Pro Glu Asn His Phe Val Ile Glu Ile
Gln Lys Asn Ile Asp Cys Met Ser Gly Pro Cys Pro Phe Gly Glu Val
65 70 75 80
Gln Leu Gln Pro Ser Thr Ser Leu Leu Pro Thr Leu Asn Arg Thr Phe 85 90 95
Ser Ile Pro Arg Leu Arg Gln Ile Gly Pro Gly Glu Ser Cys Pro Asp
115 120 125
Gly Val Thr His Ser Ile Ser Gly Arg Ile Asp Ala Thr Val Val Arg
130 135 140
Ile Gly Thr Phe Cys Ser Asn Gly Thr Val Ser Arg Ile Lys Met 145 150 155
<210> 267
<211> 9
<212> PRT
<213> Homo sapiens
<400> 267
Phe Val Arg Asp Pro Phe Val Arg Leu
<210> 268
<211> 13
<212> PRT
<213> Homo sapiens
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Phe Leu Phe Val Arg Asp Pro Phe Val Arg Leu Ile Ser

<210> 269

<400> 268

<211> 15 <212> PRT

<213> Homo sapiens

Phe Leu Phe Val Arg Asp Pro Phe Val Arg Leu Ile Ser Ala Phe
1 5 10 15

<210> 270

<211> 380

<212> PRT

<213> Homo sapiens

<400> 270

Tyr Leu His Thr Ser Phe Ser Arg Pro His Thr Gly Pro Pro Leu Pro 1 5 10 15

Thr Pro Gly Pro Asp Arg Asp Arg Glu Leu Thr Ala Asp Ser Asp Val 20 25 30

Asp Glu Phe Leu Asp Lys Phe Leu Ser Ala Gly Val Lys Gln Ser Asp 35 40 45

Leu Pro Arg Lys Glu Thr Glu Gln Pro Pro Ala Pro Gly Ser Met Glu 50 60

Glu Asn Val Arg Gly Tyr Asp Trp Ser Pro Arg Asp Ala Arg Arg Ser 65 70 75 80

Pro Asp Gln Gly Arg Gln Gln Ala Glu Arg Arg Ser Val Leu Arg Gly 85 90 95

Phe Cys Ala Asn Ser Ser Leu Ala Phe Pro Thr Lys Glu Arg Ala Phe 100 105 110

Asp Asp Ile Pro Asn Ser Glu Leu Ser His Leu Ile Val Asp Asp Arg 115 120 125

His Gly Ala Ile Tyr Cys Tyr Val Pro Lys Val Ala Cys Thr Asn Trp 130 135 140

Lys Arg Val Met Ile Val Leu Ser Gly Ser Leu Leu His Arg Gly Ala 145 150 155 160

Pro Tyr Arg Asp Pro Leu Arg Ile Pro Arg Glu His Val His Asn Ala 165 170 175

Ser Ala His Leu Thr Phe Asn Lys Phe Trp Arg Arg Tyr Gly Lys Leu 180 185 190

Ser Arg His Leu Met Lys Val Lys Leu Lys Lys Tyr Thr Lys Phe Leu 195 200 205

Phe Val Arg Asp Pro Phe Val Arg Leu Ile Ser Ala Phe Arg Ser Lys 210 215 220

Phe Glu Leu Glu Asn Glu Glu Phe Tyr Arg Lys Phe Ala Val Pro Met 225 230 235 240

Leu Arg Leu Tyr Ala Asn His Thr Ser Leu Pro Ala Ser Ala Arg Glu 245 250 255

Ala Phe Arg Ala Gly Leu Lys Val Ser Phe Ala Asn Phe Ile Gln Tyr 260 265 270 '

Leu Leu Asp Pro His Thr Glu Lys Leu Ala Pro Phe Asn Glu His Trp 275 280 285

Arg Gln Val Tyr Arg Leu Cys His Pro Cys Gln Ile Asp Tyr Asp Phe 290 295 300

Val Gly Lys Leu Glu Thr Leu Asp Glu Asp Ala Ala Gln Leu Leu Gln 305 310 315 320

Leu Leu Gln Val Asp Arg Gln Leu Arg Phe Pro Pro Ser Tyr Arg Asn 325 330 335

Ala Trp Arg Gln Gln Leu Tyr Lys Leu Tyr Glu Ala Asp Phe Val Leu 355 360 365

Phe Gly Tyr Pro Lys Pro Glu Asn Leu Leu Arg Asp 370 375 380

<210> 271

<211> 274 <212> PRT

<213> Homo sapiens

<400> 271

Lys Leu Val Arg Leu Gln Val Pro Val Arg Asn Ser Arg Val Asp Pro 1 5 10 15

Arg Val Arg Ser Lys Ile Gly Ser Arg Arg Trp Met Leu Gl<br/>n Leu Ile 20 \$25\$

Met Gln Leu Cly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly Cys 35 40 45

Phe Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg Lys 50 55 60

Pro Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala Val 65 70 75 80

Leu Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe Ala 85 90 95

Leu Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr Ile 100 105 110

Gly Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr Ser 115 120 125

Arg Thr Val Ala Ile Ile Gly Gly Phe Leu Val Leu Ala Ser Gly Ala 130 135 140

Gly Glu Leu Tyr Arg Arg Lys Pro Arg Ser Arg Ser Leu Gln Ser Thr 145 150 155 160

Gly Gin Val Phe Leu Gly Ile Tyr Leu Ile Cys Val Ala Tyr Ser Leu 165 170 175

Gln His Ser Lys Glu Asp Arg Leu Ala Tyr Leu Asn His Leu Pro Gly 180 185 190

Gly Glu Leu Met Ile Gln Leu Phe Phe Val Leu Tyr Gly Ile Leu Ala 195 200 . 205

Leu Ala Phe Leu Ser Gly Tyr Tyr Val Thr Leu Ala Ala Gln Ile Leu 210 215 220

Ala Val Leu Leu Pro Pro Val Met Leu Leu Ile Asp Gly Asn Val Ala 225 230 235 240

Leu Gly Glu Ser Val Gly Ile Phe Gly Thr Ala Val Ile Leu Ala Thr 260 265 270

Asp Gly

<210> 272

<211> 203

<212> PRT

<213> Homo sapiens

<400> 272

Met Gln Leu Gly Ser Val Leu Leu Thr Arg Cys Pro Phe Trp Gly Cys

1 5 10 15

Phe Ser Gln Leu Met Leu Tyr Ala Glu Arg Ala Glu Ala Arg Arg Lys

Pro Asp Ile Pro Val Pro Tyr Leu Tyr Phe Asp Met Gly Ala Ala Val  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Leu Cys Ala Ser Phe Met Ser Phe Gly Val Lys Arg Arg Trp Phe Ala  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Leu Gly Ala Ala Leu Gln Leu Ala Ile Ser Thr Tyr Ala Ala Tyr Ile 65 70 75 80

Gly Gly Tyr Val His Tyr Gly Asp Trp Leu Lys Val Arg Met Tyr Ser 85 90 95

Arg Thr Val Ala Ile Ile Gly Gly Phe Leu Val Leu Ala Ser Gly Ala 100 105 110

Gly Glu Leu Tyr Arg Arg Lys Pro Arg Ser Arg Ser Leu Gln Ser Thr

120 Gly Gln Val Phe Leu Gly Ile Tyr Leu Ile Cys Val Ala Tyr Ser Leu 130 135 140 Gln His Ser Lys Glu Asp Arg Leu Ala Tyr Leu Asn His Leu Pro Gly 145 150 155 160 Gly Glu Leu Met lle Gln Leu Phe Phe Val Leu Tyr Gly Ile Leu Ala 165 170 175 Pro Gly Leu Ser Val Arg Leu Leu Arg Asp Pro Arg Cys Pro Asp Pro 180 185 190 Gly Cys Thr Ala Ala Pro Cys His Ala Ala His 195 200 <210> 273 <211> 407 <212> PRT <213> Homo sapiens Ser Asn Glu Ile Leu Leu Ser Phe Pro Gln Asn Tyr Tyr Ile Gln Trp 1 5 10 15 Leu Asn Gly Ser Leu Ile His Gly Leu Trp Asn Leu Ala Ser Leu Phe 20 25 30Ser Asn Leu Cys Leu Phe Val Leu Met Pro Phe Ala Phe Phe Leu 35 40 45 Glu Ser Glu Gly Phe Ala Gly Leu Lys Lys Gly Ile Arg Ala Arg Ile 50 55 60 Leu Glu Thr Leu Val Met Leu Leu Leu Leu Ala Leu Leu Ile Leu Gly 65 70 75 80 Ile Val Trp Val Ala Ser Ala Leu Ile Asp Asr. Asp Ala Ala Ser Met 85 90 95 Glu Ser Leu Tyr Asp Leu Trp Glu Phe Tyr Leu Pro Tyr Leu Tyr Ser 100 105 . 110Cys Ile Ser Leu Met Gly Cys Leu Leu Leu Leu Cys Thr Pro Val 115 120 125 Gly Leu Ser Arg Met Phe Thr Val Met Gly His Leu Leu Val Lys Pro . 130 135 140 Thr Ile Leu Glu Asp Leu Asp Glu Gln Ile Tyr Ile Ile Thr Leu Glu 145 150 155 160 Glu Glu Ala Leu Gln Arg Arg Leu Asn Gly Leu Ser Ser Ser Val Glu 155 170 175

Tyr Asn Ile Met Glu Leu Glu Gln Glu Leu Glu Asn Val Lys Thr Leu 180 185 190 Lys Thr Lys Leu Clu Arg Arg Lys Lys Ala Ser Ala Trp Glu Arg Asn 195 200 205

Leu Val Tyr Pro Ala Val Met Val Leu Leu Leu Ile Glu Thr Ser Ile 210 215 220

Scr Val Leu Leu Val Ala Cys Asn Ile Leu Cys Leu Leu Val Asp Glu 225 230 235 240

Thr Ala Met Pro Lys Gly Thr Arg Cly Pro Gly Ile Gly Asn Ala Ser 245 250 255

Leu Ser Thr Phe Gly Phe Val Gly Ala.Ala Leu Glu Ile Ile Leu Ile 260 265 270

Phe Tyr Leu Met Val Ser Ser Val Val Gly Phe Tyr Ser Leu Arg Phe 275 280 285

Phe Gly Asn Phe Thr Pro Lys Lys Asp Asp Thr Thr Met Thr Lys Ile 290 295 300

Ile Gly Asn Cys Val Ser Ile Leu Val Leu Ser Ser Ala Leu Pro Val 305 310 310 320

Met Ser Arg Thr Leu Gly Ile Thr Arg Phe Asp Leu Leu Gly Asp Phe 325 330 335

Gly Arg Phe Asn Trp Leu Gly Asn Phe Tyr Ile Val Leu Ser Tyr Asn  $340 \hspace{1cm} 345 \hspace{1cm} 350$ 

Leu Leu Phe Ala Ile Val Thr Thr Leu Cys Leu Val Arg Lys Phe Thr 355 360 365

Ser Ala Val Arg Glu Glu Leu Phe Lys Ala Leu Gly Leu His Lys Leu 370 375 380

His Leu Pro Asn Thr Ser Arg Asp Ser Glu Thr Ala Lys Pro Ser Val 385 390 395 400

Asn Gly His Gln Lys Ala Leu 405

<210> 274

<211> 165

<212> PRT

<213> Homo sapiens

<400> 274

Arg Ser Tyr Met Gln Ser Val Trp Thr Glu Glu Ser Gln Cys Thr Leu  $1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15$ 

Leu Asn Ala Ser Ile Thr Glu Thr Phe Asn Cys Ser Phe Ser Cys Gly 20 25 30

Pro Asp Cys Trp Lys Leu Ser Gln Tyr Pro Cys Leu Gln Val Tyr Val 35 40 45

Asn Leu Thr Ser Ser Gly Glu Lys Leu Leu Tyr His Thr Glu Glu 50 60

Thr Ile Lys Ile Asn Gln Lys Cys Ser Tyr Ile Pro Lys Cys Gly Lys 65 70 75 80

Asn Phe Glu Glu Ser Met Ser Leu Val Asn Val Val Met Glu Asn Phe 85 90 . 95

Arg Lys Tyr Gln His Phe Ser Cys Tyr Ser Asp Pro Glu Gly Asn Gln 100 105 110

Lys Ser Val Ile Leu Thr Lys Leu Tyr Ser Ser Asn Val Leu Phe His 115 120 . 125

Ser Leu Phe Trp Pro Thr Cys Met Net Ala Gly Gly Val Ala Ile Val 130 135 140

Ala Met Val Lys Leu Thr Gln Tyr Leu Ser Leu Leu Cys Glu Arg Ile 145 150 155 160

Gln Arg Ile Asn Arg 165

<210> 275

<211> 155

<212> PRT

<213> Homo sapiens

<400> 275

Ala Phe Ala His Leu Gln Leu Gly Pro Met Trp Lys Leu Trp Arg Ala 1 5 10 15

Glu Glu Gly Ala Ala Ala Leu Gly Gly Ala Leu Phe Leu Leu Leu Phe 20 25 30

Ala Leu Gly Val Arg Gln Leu Leu Lys Gln Arg Arg Pro Met Gly Phe  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Pro Pro Gly Pro Pro Gly Leu Pro Phe Ile Gly Asn Ile Tyr Ser Leu 50 55 60

Ala Ala Ser Ser Glu Leu Pro His Val Tyr Met Arg Lys Gln Ser Gln 65 70 75 80

Val Tyr Gly Glu Val Gln Pro Arg Arg Ala Pro Gly Arg Glu Gly Arg 85 90 95

Gln Ala Gly Pro Gly Trp Pro Gly Pro Ser Trp Leu Asp Leu Trp Pro 100 105 110

Pro Leu Gly Arg Leu Val Gly Thr Ser Pro Cys Ala Gly Cys Pro Leu 115 120 125

Arg Asp Thr Arg Phe Pro Gly Leu Glu Gly Arg Ser Pro Arg Arg 130 135 140

Ala Pro Leu Gln Gly Glu Pro Arg Pro Cys Arg

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145
                       150
                                              155
<210> 276
<211> 42
<212> PRT
<213> Homo sapiens
 <400> 276
Met Arg Val Arg Ile Gly Leu Thr Leu Leu Leu Cys Ala Val Leu Leu
1 5 16 15
Ser Leu Ala Ser Ala Ser Ser Asp Glu Glu Gly Ser Gln Asp Glu Ser 20 25.
Leu Gly Phe Gln Asp Tyr Phe Asp Ile Arg 35 \sim 40
<210> 277
<211> 155
<212> PRT
<213> Homo sapiens
<400> 277
Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly ^{1} 5 10 15
Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly 20 25 30
Thr Ala Pro Cys, Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys 35 40 45
Cys Met Asp Cys Ser Thr Ser Cys Pro Leu Pro Ala Ala Leu Ala His
Pro Trp Gly Arg Ser Glu Pro Asp Leu Arg Ala Gly Ala Ala Phe Trp 65 70 75 80
Leu Phe Gly Leu Glu Thr Met Pro Gln Glu Arg Glu Val His His Pro
His Arg Gly Asp Arg Arg Gly Leu Pro Ser Cys Gly Ala Asp Pro 100 105 110
Val Thr Met Cys Pro Leu Pro Ala Gly Ala Arg Pro Leu Ile Ile His
115 120 125
Ser Ser Ile Leu Glu Pro Val Ser Ala Ser Gln Thr Arg Arg Glu Pro
Ser Ser Ser Asn His Lys Gly Gly Gly Gly Arg
145 150 155
```

<210> 278 <211> 207 <212> PRT

<213> Homo sapiens

Gly Thr Ser Phe Leu Asp Pro Thr Leu Ser Leu Phe Val Leu Glu Lys
1 5 20 15

Phe Asn Leu Pro Ala Gly Tyr Val Gly Leu Val Phe Leu Gly Met Ala 20 25 30

Leu Ser Tyr Ala Ile Ser Ser Pro Leu Phe Gly Leu Leu Ser Asp Lys 35 40 45

Arg Pro Pro Leu Arg Lys Trp Leu Leu Val Phe Gly Asn Leu Ile Thr 50 55 . 60

Ala Gly Cys Tyr Met Leu Leu Gly Pro Val Pro Ile Leu His Ile Lys 65 70 75 80

Ser Gln Leu Trp Leu Leu Val Leu Ile Leu Val Val Ser Gly Leu Ser 85 90 95

Ala Cly Met Ser Ile Ile Pro Thr Phe Pro Glu Ile Leu Ser Cys Ala 100 105 110

His Glu Asn Gly Phe Glu Glu Gly Leu Ser Thr Leu Gly Leu Val Ser 115 120 125

Gly Leu Phe Ser Ala Met Trp Ser Ile Gly Ala Phe Met Gly Pro Thr 130 135 140

Leu Gly Gly Phe Leu Tyr Glu Lys Ile Gly Phe Glu Trp Ala Ala 145 150 155 160

Ile Gln Gly Leu Trp Ala Leu Ile Ser Gly Leu Ala Met Gly Leu Phe 165 170 175

Tyr Leu Leu Glu Tyr Ser Arg Arg Lys Arg Ser Lys Ser Gln Asn Ile 180 185 190

Leu Ser Thr Glu Glu Glu Arg Thr Thr Leu Leu Pro Asn Glu Thr 195 200 205

<210> 279

<211> 85

<212> PRT

<213> Homo sapiens

Gly Thr Arg Glu Ala Arg Leu Arg Asp Leu Thr Arg Phe Tyr Asp Lys

1 5 10 15

Val Leu Ser Leu His Glu Asp Ser Thr Thr Pro Val Ala Asn Pro Leu 20 25 30

Leu Ala Pho Thr Leu Ile Lys Arg Leu Gln Ser Asp Trp Arg Asn Val  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Val His Ser Leu Glu Ala Ser Glu Asn Ile Arg Ala Leu Lys Asp Gly

50

Tyr Glu Lys Val Glu Gln Asp Leu Pro Ala Phe Glu Asp Leu Glu Gly

Ala Ala Arg Ala Leu

<210> 280

<211> 7 <212> PRT

<213> Homo sapiens

<400> 280

Ala Leu Met Arg Leu Gln Asp 1 5

<210> 281 <211> 7

<212> PRT

<213> Homo sapiens

<400> 281

Val Glu Ala Gly Gly Ala Thr 1 5

<210> 282

<211> 489

<212> PRT

<213> Homo sapiens

<400> 282

Gly Thr Arg Glu Ala Arg Leu Arg Asp Leu Thr Arg Phe Tyr Asp Lys

1 10 15

Val Leu Ser Leu His Glu Asp Ser Thr Thr Pro Val Ala Asn Pro Leu 20 25 30

Leu Ala Phe Thr Leu Ile Lys Arg Leu Gln Ser Asp Trp Arg Asn Val

Val His Ser Leu Glu Ala Ser Glu Asn Ile Arg Ala Leu Lys Asp Gly 50 55 60

Tyr Glu Lys Val Glu Gln Asp Leu Pro Ala Phe Glu Asp Leu Glu Gly 65 70 75 80

Ala Ala Arg Ala Leu Met Arg Leu Gln Asp Val Tyr Met Leu Asn Val 85 90 95

Lys Gly Leu Ala Arg Gly Val Phe Gln Arg Val Thr Gly Ser Ala Ile 105

Thr Asp Leu Tyr Ser Pro Lys Arg Leu Phe Ser Leu Thr Gly Asp Asp 115 120 125

Cys Phe Gln Val Gly Lys Val Ala Tyr Asp Met Gly Asp Tyr Tyr His 130 135 140

Ala Ile Pro Trp Leu Giu Glu Ala Val Ser Leu Phe Arg Gly Ser Tyr 145 150 155 160

Gly Glu Trp Lys Thr Glu Asp Glu Ala Ser Leu Glu Asp Ala Leu Asp 165 170 175

His Leu Ala Phe Ala Tyr Phe Arg Ala Gly Asn Val Ser Cys Ala Leu 180 185 190

Ser Leu Ser Arg Glu Phe Leu Leu Tyr Ser Pro Asp Asn Lys Arg Met 195 200 . . . 205

Ala Arg Asn Val Leu Lys Tyr Glu Arg Leu Lou Ala Glu Ser Pro Asn 210 /215 220

His Val Val Ala Glu Ala Val Ile Gln Arg Pro Asn Ile Pro His Leu 225 230 235 240

Gln Thr Arg Asp Thr Tyr Glu Gly Leu Cys Gln Thr Leu Gly Ser Gln 245 250 255

Pro Thr Leu Tyr Gln Ile Pro Ser Leu Tyr Cys Ser Tyr Glu Thr Asn 260 265 270

Ser Asn Ala Tyr Leu Leu Leu Gln Pro Ile Arg Lys Glu Val Ile His 275 280 285

Leu Gl: Pro Tyr Ile Ala Leu Tyr His Asp Phe Val Scr Asp Ser Glu 290 295 300

Ala Gln Lys Ile Arg Glu Leu Ala Glu Pro Trp Leu Gln Arg Ser Val 305 310 315 320

Val Ala Ser Gly Glu Lys Gln Leu Gln Val Glu Tyr Arg Ile Ser Lys 325 330 335

Ser Ala Trp Leu Lys Asp Thr Val Asp Leu Lys Leu Val Thr Leu Asn 340 345 350

His Arg Ile Ala Ala Leu Thr Gly Leu Asp Val Arg Pro Pro Tyr Ala 355 . 360 865

Glu Tyr Leu Gln Val Val Asn Tyr Gly Ile Gly Cly His Tyr Glu Pro 370 380

His Phe Asp His Ala Thr Ser Pro Ser Ser Pro Leu Tyr Arg Met Lys 385 390 395 400

Ser Gly Asn Arg Val Ala Thr Phe Met Ile Tyr Leu Ser Ser Val Glu 405 410 415

Ala Gly Gly Ala Thr Ala Phe Ile Tyr Ala Asn Leu Ser Val Pro Val 420 425 430

Val Arg Asn Ala Ala Leu Phe Trp Trp Asn Leu His Arg Ser Gly Glu 435 440 445

Gly Asp Ser Asp Thr Leu His Ala Gly Cys Pro Val Leu Val Gly Asp 450 455 460

Lys Trp Val Ala Asn Lys Trp Ile His Glu Tyr Gly Gln Glu Phe Arg 465 470 475 480

Arg Pro Cys Ser Ser Ser Pro Glu Asp

<210> 283

<211> 136 <212> PRT

<213> Homo sapiens

The Gln Pro Ser His Ala Ala Leu Leu His Cys Arg Ser Thr Phe Arg

1 5 10 15

Lys Thr Glu Cys Leu Asp Pro Trp Trp Val Arg Arg Gln Leu Leu Gly 20 25 30

Met Ala Gly Ile Gly Gly Leu Gln Lys Met Lys Ala Pro His Thr Gly  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Val Leu His Leu Cly Ser Val Trp Val Phe Leu Cly Pro Phe Leu Leu 50 55 60

Gly Val Gly Tyr Thr Leu Thr Phe Asn Pro Leu Ser Gly Cys Met Ser 65 70 75 80

Thr Val Arg Trp Leu Asn Ser Asn Ile Thr Ala Asn Arg Thr Leu Ser 85 90 95

Arg Ser Val Cys His Val Thr Pro Leu His Arg Ser Leu Ser Pro His 100 . 105 110

Asp Gly Glu Tyr Leu Arg Gln Met Leu Leu Asn Ser Ser Ser Arg Ala 115 120 125

Gly Glu Ala Gly Ser Trp Gly Tyr 135

<210> 284

<211> 86

<212> PRT

<213> Homo sapiens

<400> 284

Cys Ser Ser Pro Pro Gly Arg Leu Pro Trp Cys Trp Thr Ala Pro Arg 1 5° 10 15

Thr Leu Gly Lys His Gly Ser Leu Ile Ser Thr Leu Arg Leu Thr Ala 20 25 30

Pro Leu His Leu Ala Trp Lys Met Met Leu Ser Arg Lys Ala Leu Phe . 35 40 45

Val Leu Leu Asn Thr Pro Val Leu Phe His Ala Leu Glu Gly Arg Leu 50 55 60

Phe Ser Lys Leu Cys His His His Thr Ile Gln Arg Thr Leu Thr Val 65 70 75 80

Pro Lys Phe Arg Ser Ser 85

<210> 285

<211> 75

<212> PRT

<213> Homo sapiens

<400> 285

Arg Ser Pro Thr Ser Arg Val Gln Leu Leu Lys Arg Gln Ser Cys Pro

1 5 10 15

Cys Gln Arg Asn Asp Leu Asn Glu Glu Pro Gln His Phe Thr His Tyr 20 25 30

Ala Ile Tyr Asp Phe Ile Val Lys Gly Ser Cys Phe Cys Asn Gly His  $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$ 

Ala Asp Gln Cys Ile Pro Val His Gly Phe Arg Pro Val Lys Ala Pro  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Gly Thr Phe His Met Val His Gly Lys Cys Met 65 70 75

<210> 286

<211> 296

<212> PRT

<213> Homo sapiens

<400> 286

His Asn Thr Ala Gly Ser His Cys Gln His Cys Ala Pro Leu Tyr Asn 1 5 10 15

Asp Arg Pro Trp Glu Ala Ala Asp Gly Lys Thr Gly Ala Pro Asn Glu 20 25 30

Cys Arg Thr Cys Lys Cys Asn Gly His Ala Asp Thr Cys His Phe Asp  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Val Asn Val Trp Glu Ala Ser Gly Asn Arg Ser Gly Gly Val Cys Asp 50 55 60

Asp Cys Gln His Asn Thr Glu Gly Gln Tyr Cys Gln Arg Cys Lys Pro 65 70 75 80

Gly Phe Tyr Arg Asp Leu Arg Arg Pro Phe Ser Ala Pro Asp Ala Cys 85 90 95

Lys Pro Cys Ser Cys His Pro Val Gly Ser Ala Val Leu Pro Ala Asn 100 105 110 Ser Val Thr Phe Cys Asp Pro Ser Asn Gly Asp Cys Pro Cys Lys Pro 115 120 125

Gly Val Ala Gly Arg Arg Cys Asp Arg Cys Met Val Gly Tyr Trp Gly 130 135 140

Phe Gly Asp Tyr Gly Cys Arg Pro Cys Asp Cys Ala Gly Ser Cys Asp 145 150 150 155

Pro Ile Thr Gly Asp Cys Ile Ser Ser His Thr Asp Ile Asp Trp Tyr 165 170 175

His Glu Val Pro Asp Phe Arg Pro Val His Asn Lys Ser Glu Pro Ala 180 185 190

Trp Glu Trp Glu Asp Ala Gln Gly Phe Ser Ala Leu Leu His Ser Gly 195 200 205

Lys Cys Glu Cys Lys Glu Gln Thr Leu Gly Asn Ala Lys Ala Phe Cys 210 215 220

Gly Met Lys Tyr Ser Tyr Val Leu Lys Ile Lys Ile Leu Ser Ala His 225 230 . 235 240

Asp Lys Gly Thr His Val Glu Val Asn Val Lys Ile Lys Lys Val Leu 245 250 255

Arg Ile Met Asp Gly Gln Arg Met His Leu Ser Asn Pro Gln Ser Trp 280

Phe Gly Ile Pro Cys Ser Arg Thr 290 295

<210> 287 <211> 37

<212> PRT

<213> Homo sapiens

Cys Asp Asp Cys Gln His Asn Thr Glu Gly Gln Tyr Cys Gln Arg Cys

1 5 10 15

Lys Pro Gly Phe Tyr Arg Asp Leu Arg Arg Pro Phe Ser Ala Pro Asp 20 25 30

Ala Cys Lys Pro Cys

<210> 288

<211> 36

<212> PRT

<213> Homo sapiens

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194

<400> 288 Cys Pro Cys Lys Pro Gly Val Ala Gly Arc Arg Cys Asp Arg Cys Met
1 5 15

Val Gly Tyr Trp Gly Phe Gly Asp Tyr Gly Cys Arg Pro Cys Asp Cys 20 25 30

Ala Gly Ser Cys 35

<210> 289

<211> 66 <212> PRT

<213> Homo sapiens

<400> 289

Asn I'le Ser Ser Gln Tyr Cys Ile Leu Lys Ser Leu Glu Met Met Ile 1 5 10 15

Ser Gly Leu Lys Leu Leu Val Leu Phe Leu Lys Phe Ala Pro Glu Asn 20 25 30

Tyr Cys Leu Ser Thr Glu Thr Leu Gln Met Pro Asn Arg His Leu Arg 35 40 45

Leu Ser Lys Ala Thr Cys Tyr Leu Met Lys Cys Leu Leu Pro Ser Tyr 50 55 60

Phe Glu 65

<210> 290

<211> 88

<212> PRT

<213> Homo sapiens

<400> 290

Pro Ile Glu Gly Thr Pro Ala Gly Thr Gly Prc Glu Phe Pro Gly Arg

1 5 10 15

Pro Thr Arg Pro Gln Arg Met Arg Ser Leu Ile Ser Ser His Pro Cys 20 25 30

Gln His Leu Leu Leu Leu Leu Leu Leu Leu Pho Leu Ile Leu Ala Ile  $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$ 

Leu Val Asp Val Lys Trp Tyr Leu Val Leu Phe Ile Cys Ile Ser Leu 50 60

Met Thr Ser Asp Val Glu His Leu Phe Met Cys Leu Leu Ala Ile Arg 65 70 75 80

Ile Ser Ser Trp Arg Asn Val Tyr 95

<210> 291

<222> (55)

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<211> 60
 <212> PRT
 <213> Homo sapiens
<400> 291
Asn Trp Val Pro Thr Cys Leu Cys Pro Ser Ala Pro Cys Ser Phe His
                                       10
Leu Leu Ser Arg Phe Lys Cys Leu Phe Ser Pro Gln Arg Leu Thr Asp
Ile Phe Arg Arg Tyr Asp Thr Asp Gln Asp Gly Trp Ile Gln Val Ser
Tyr Glu Gln Tyr Leu Ser Met Val Phe Ser Ile Val
     50
                          55
<210> 292
<211> 33
<212> PRT
<213> Homo sapiens
<400> 292
Gln Arg Leu Thr Asp Ile Phe Arg Arg Tyr Asp Thr Asp Gln Asp Gly
                                      10
Trp Ile Gln Val Ser Tyr Glu Gln Tyr Leu Ser Met Val Phe Ser Ile
                                  25
Val
<210> 293
<211> 73
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
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<223> Xaa equals any of the naturally occurring L-amino acids

<213> Homo sapiens

<400> 295

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<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 293
Met Phe Tyr Lys Leu Thr Leu Ile Leu Cys Glu Leu Ser Val Ala Gly
1 10 15
Val Thr Gln Ala Ala Ser Gln Arg Pro Leu Gln Arg Leu Pro Arg His 20 \\ \hspace{1.5cm} 25 \\ \hspace{1.5cm} 30
Ile Cys Ser Gln Arg Xaa Pro Pro Gly Arg Cys Leu Leu Lys Ala Xaa 35 \hspace{1cm} 40 \hspace{1cm} . \hspace{1cm} 45
Leu Gln Thr Trp Xaa Xaa Pro Asp Lys Pro Ile Pro Arg Leu Ser
Pro Pro Leu Xaa Ser Asp Pro Lys Arg
65 70
<210> 294
<211> 95
<212> PRT
<213> Homo sapiens
<400> 294
Thr Ser Ser Pro Val Phe Ser Phe Cys Ser Met Ala Val Arg Glu Pro
Asp His Leu Gln Arg Val Ser Leu Pro Arg Tyr Asn Val Ser Ala Ser
Leu Gln Trp Leu Pro Cys His Arg Ile Val Leu Gln Pro Trp His Met 35 \hspace{1cm} 40 \hspace{1cm} 45
Cys Ala Met Trp Glu Leu Gly Gln Val Leu Phe His Pro Val Ala Pro 50 \hspace{1cm} 55 \hspace{1cm} 60
Arg Glu Gly Ala Ala Pro Ser Pro Val Ser Thr Leu Thr Trp Pro Ser 65 70 75 80
Ser Cys Ser His Ser Glu Ser Thr Met Glu Leu Glu Leu Gln Phe
85 90 95
<210> 295
<211> 16
<212> PRT
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Met Ala Val Arg Glu Pro Asp His Leu Gln Arg Val Ser Leu Pro Arg

```
<210> 296
<211> 7
 <212> PRT
 <213> Homo sapiens
 <400> 296
Leu Pro Cys His Arg Ile Val
 <210> 297
<211> 15
<212> PRT
 <213> Homo sapiens
 <400> 297
Ser Leu Gln Trp Leu Pro Cys His Arg Ile Val Leu Gln Pro Trp 1 5 10 15
<210> 298
<211> 454
<212> PRT
<213> Homo sapiens
<400> 298
Cys Phe Lys Arg Lys Pro Lys Arg Glu His Cys Ser Cys Pro Ile Thr \frac{1}{5} 10 25
Tyr Cln Ser Leu Cly Asp Ile Leu Asn Ala Ser Phe Phe Ser Lys Arg 20 25 30
Lys Gly Met Gln Glu Val Lys Leu Asn Ser Tyr Val Val Ser Gly Thr 35 40 45
Ile Gly Leu Lys Glu Lys Ile Ser Leu Ser Glu Pro Val Phe Leu Thr 50 60
Phe Arg His Asn Gln Pro Gly Asp Lys Arg Thr Lys His Ile Cys Val
65 70 75 80
Tyr Trp Glu Gly Ser Glu Gly Gly Arg Trp Ser Thr Glu Gly Cys Ser 85 90 95
His Val His Ser Asn Gly Ser Tyr Thr Lys Cys Lys Cys Phc His Leu 100 105 110
Ser Ser Phe Ala Val Leu Val Ala Leu Ala Pro Lys Glu Asp Pro Val 115 120 125
Leu Thr Val Ile Thr Gln Val Gly Leu Thr Ile Ser Leu Leu Cys Leu
                           135
Phe Leu Ala Ile Leu Thr Phe Leu Leu Cys Arg Pro Ile Gln Asn Thr
145 150 155 160
Ser Thr Ser Leu His Leu Glu Leu Ser Leu Cys Leu Phe Leu Ala His
165 170 175
```

Leu Leu Phe Leu Thr Gly Ile Asn Arg Thr Glu Pro Glu Val Leu Cys 180 185 190

Ser Ile Ile Ala Gly Leu Leu His Phe Leu Tyr Leu Ala Cys Phe Thr 195 200 205

Trp Met Leu Leu Glu Gly Leu His Leu Phe Leu Thr Val Arg Asr Seu 210 215 220

Lys Val Ala Asn Tyr Thr Ser Thr Gly Arg Phe Lys Lys Arg Phe Met 225 230 235

Tyr Pro Val Gly Tyr Gly Ile Pro Ala Val Ile Ile Ala Val Ser Ala 245 250 255

Leu Asp Lys Gly Phe Ile Trp Ser Phe Met Gly Pro Val Ala Val Ile 275 280 285

Ile Leu Ile Asn Leu Val Phe Tyr Phe Gln Val Leu Trp Ile Leu Arg 290 295 300

Ser Lys Leu Ser Ser Leu Asn Lys Glu Val Ser Thr Ile Glr Asp Thr 305 310 315 320

Arg Val Met Thr Phe Lys Ala Ile Ser Gln Leu Phe Ile Leu Gly Cys 325  $\phantom{\bigg|}$  330  $\phantom{\bigg|}$  335  $\phantom{\bigg|}$ 

Ser Trp Gly Leu Gly Phe Phe Met Val Glu Glu Val Gly Lys Thr Ile 340 \$345

Gly Ser Ile Ile Ala Tyr Ser Phe Thr Ile Ile Asn Thr Leu Gln Gly 355 360 365

Val Leu Leu Phe Val Val His Cys Leu Leu Asn Arg Gln Val Arg Met 370 380

Glu Tyr Lys Lys Trp Phe Ser Gly Met Arg Lys Gly Val Glu Thr Glu 385 390 395 400

Ser Thr Glu Met Ser Arg Ser Thr Thr Gln Thr Lys Thr Glu Glu Val 405  $\phantom{\bigg|}405$ 

Gly Lys Ser Ser Glu Ile Phe His Lys Gly Gly Thr Ala Ser Ser Ser 420 425 410

Ala Glu Ser Thr Lys Gln Pro Gln Pro Gln Val His Leu Val Ser Ala 435 440 445

Ala Trp Leu Lys Met Asn 450

<210> 299

<211> 101

<212> PRT

199

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<213> Homo sapiens
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<400> 299

Phe Phe Trp Lys Glu Asn Leu Arg Arg Asn Gly Ser Arg Clu Asp Phe

Ala Arg Arg Ala Thr Gln Leu Ile Gln Ser Val Glu Leu Ser Ile Try 20 25 30

Asn Ala Ser Phe Ala Ser Pro Gly Lys Gly Gln Ile Ser Glu Phe Asp  $15 \hspace{1cm} 40 \hspace{1cm} 45$ 

Ile Val Tyr Glu Thr Lys Arg Cys Asn Glu Thr Arg Glu Asn Ala Phe  $50 \ \ 55 \ \ \ 60$ 

Leu Glu Ala Gly Asn Asn Thr Met Asp Ile Asn Cys Ala Asp Ala Leu

Lys Gly Asn Leu Arg Glu Ser Thr Ala Val Ala Leu Ser Leu Ile Asn R5  $90 \ \ 95$ 

Leu Leu Gly Ile Phe 100

<210> 300

<211> 27 <212> PRT

<213> Homo sapiens

<400> 300

Asp Ile Asn Glu Cys Glu Thr Gly Leu Ala Lys Cys Lys Tyr Lys Ala 1 5 10 15

Tyr Cys Arg Asn Lys Val Gly Gly Tyr Ile Cys  $20 \ \ 25$ 

<210> 301

<211> 12 <212> PRT

<213> Homo sapiens

<400> 301

Cys Arg Asn Lys Val Gly Gly Tyr Ile Cys Ser Cys 1 5 10

<210> 302

<211> 331 <212> PRT

<213> Homo sapiens

<400> 302

Ala Leu Cys Pro His Pro His Leu Ile Leu Asn Val Thr Val Ser Pro

Ala Pro Ser Cys Arg His Val Lys Lys Val Val Ala Ser Pro Ser Pro 20 25 30

Ser	Thi	Th:	r Mei	: Ile	Ala	Het	Asp 40		Pro	His	Ser	Lys 45		Ala	Le
Asp	Se <sub>1</sub>	r Ile	e Ası	ı Glu	Leu	Pro 55	Glu	Asn	Ile	Leu	Leu 60		Leu	Phe	Th
H1s 65	Val	Pro	o Ala	Arg	Gln 70	Leu	Leu	Leu	Asn	Cys 75	Arg	Leu	Val	Cys	Se 8
Leu	Trp	Arg	y Asr	Leu 85	Ile	Asp	Leu	Met	Thr 90	Leu	Trp	Lys	Arg	Lуз 95	
Leu	Arg	Glu	1 Gly	Phe	Ile	Thr	Lys	Asp 105	тр	Asp	. Gln	Pro	Val 110	Ala	As
Trp	Lys	11e	Phe	туг	Phe	Leu	Arg 120	Ser	Leu	His	Arg	Asn 125	Leu	Leu	Ār
Asn	Pro 130	Cys	: Ala	Glu	Glu	Asp 135	Met	Phe	Ala	Trp	Gln 140	Ile	Asp	Phe	Ası
Gly 145	Gly	Asp	Arg	Trp	Lys 150	Val	Glu	Ser	Leu	Pro 155	Gĺy	Ala	His	Gly	Th:
Asp	Phe	Pro	Asp	Pro 165	Lys	Val	Lys	Lys	<b>Tyr</b> 170	Phe	Val	Thr	Ser	Tyr 175	Glu
Met	Cys	Leu	Lys 180	Ser	Gln	Leu	Val	Asp 185	Leu	Va:	Ala	Glu	Gly 190	Tyr	Tr
Glu	Glu	Leu 195	Leu	Asp	Thr	Phe	Arg 200	Pro	Asp	Ile	Val	Val 205	Lys	Asp	Tr
Phe	Àla 210	Ala	Arg	Äla	Ąsp	Cys 215	Gly	Суs	Thr	Tyr	Gln 220	Leu	Lys	Val	Glr
Leu 225	λla	Ser	Ala	Asp	Туг 230	Phe	Val	Leu	Ala	Ser 235	Phe	Glu	Pro	Pro	Pro 240
Val	Thr	Ile	Gln	Gln 245	Trp	Asn	Asn	Ala	Thr 250	Trp	Thr	Glu	Val	Ser 255	Tyr
Thr	Phe	Ser	Asp 260	Tyr	Pro	Arg	Gly	Val 265	Arg	Tyr	Ile	Leu	Phe 270	Gln	His
Gly	G1y	Arg 275	Asp	Thr	Gln	Σyr	Trp 280	Ala	Gly	Trp	Tyr	Gly 285	Pro	Arg	Val
Thr	Asn 290	Ser	Ser	Ile	Val	Val 295	Ser	Pro	Lys		Thr 300	Arg	Asn	Gln	Ala
Ser 305	Ser	Glu	Ala	Gla	Pro (	Gly	Gln	Lys	His	Gly 315	Gln	Glu	Glu		Ala 320
Gln	Ser	Pro	Tyr	Ary . 325	Ala '	Val '	Val (		Ile 330	Phe					

<210> 303 <211> 328 <212> PRT

<213> Homo sapiens

Arg Gln Arg Ser Trp Asn Pro Gly Thr Asn Cys Tyr His Pro Asn Met

1 10 15

Pro Asp Ala Phe Leu Thr Cys Glu Thr Val Ile Phe Ala Trp Ala Ile 20 25 30

Gly Glu Glu Phe Ser Tyr Pro Pro His Val Gly Leu Ser Leu Gly 35 40 45

Pro Thr Tyr Glu Glu Gly Leu Ile Asp Asr. Ser Gly Leu Arg Leu Phe 65 70 75 80

Tyr Thr Met Asp Ile Arg Lys Tyr Asp Ala Gly Val Ile Glu Ala Gly 85 90 95

Leu Trp Val Ser Leu Phe His Thr Ile Pro Pro Gly Met Pro Glu Phe 100 100 110

Ala Glu Lys Pro Ser Gly Ile His Val Phe Ala Val Leu Leu His Ala 130 135 140

His Leu Ala Gly Arg Gly Ile Arg Leu Arg His Phe Arg Lys Gly Lys 145 150 155 160

Glu Met Lys Leu Leu Ala Tyr Asp Asp Asp Phe Asp Phe Asn Phe Gln 165 170 175

Glu Phe Gln Tyr Leu Lys Glu Glu Gln Thr Ile Leu Pro Gly Asp Asn 180 185 190

Leu Ile Thr Glu Cys Arg Tyr Asn Thr Lys Asp Arg Ala Glu Met Thr 195  $\phantom{\bigg|}200\phantom{\bigg|}$ 

Trp Gly Gly Leu Ser Thr Arg Ser Glu Met Cys Leu Ser Tyr Leu Leu 210 215 220

Tyr Tyr Pro Arg Ile Asn Leu Thr Arg Cys Ala Ser Ile Pro Asp Ile 225 230 235 240

Met Glu Gln Lee Gln Phe Ile Gly Val Lys Glu Ile Tyr Arg Pro Val 245 250 255

Thr Thr Trp Pro Phe Ile Ile Lys Ser Pro Lys Gln Tyr Lys Asn Leu 260 255 270

Ser Phe Met Asp Ala Met Asn Lys Phe Lys Trp Thr Lys Lys Glu Gly 275 280 285

Leu Ser Phe Asn Lys Leu Val Leu Ser Leu Pro Val Asn Val Arg Cys 290 295 300

Ser Lys Thr Asp Asn Ala Glu Trp Ser Ile Pro Arg Asn Asp Ser Ile 305 310 315 320

Thr Ser Arg Tyr Arg Lys Thr Leu 325

<210> 304

<211> 272

<212> PRT

<213> Homo sapiens

Met Cys Cys Trp Pro Leu Leu Leu Trp Gly Leu Leu Pro Gly Thr 1 5 10 25

Ala Ala Gly Gly Ser Gly Arg Thr Tyr Pro His Arg Thr Leu Leu Asp 20 25 30

Ser Glu Gly Lys Tyr Trp Leu Gly Trp Ser Gln Arg Gly Ser Gln Ile  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Ser Pro Thr Gly Ala Met Ala Ser Ala Asp Ile Val Val Gly Gly Val 65 70 75 80

Ala His Gly Arg Pro Tyr Leu Gln Asp Tyr Phc Thr Asn Ala Asn Arg 85 90 95

Glu Leu Lys Lys Asp Ala Gln Gln Asp Tyr His Leu Glu Tyr Ala Met 100 105 110

Glu Asn Ser Thr His Thr Ile Ile Glu Phe Thr Arg Glu Leu His Thr 115 120 125

Cys Asp Ile Asn Asp Lys Ser Ile Thr Asp Ser Thr Val Arg Val Ile 130  $$135\$ 

Trp Ala Tyr His His Glu Asp Ala Gly Clu Ala Gly Pro Lys Tyr His 145 150 155 160

Asp Ser Asn Arg Gly Thr Lys Ser Leu Arg Leu Leu Asn Pro Glu Lys 165 170 175

Thr Ser Val Leu Ser Thr Ala Leu Pro Tyr Phe Asp Leu Val Asn Gln 180 185 190

Asp Val Pro Ile Pro Asn Lys Asp Thr Thr Tyr Trp Cys Gln Met Phe 195 200 205

Lys Ile Pro Val Phe Gln Glu Lys His His Val Ile Lys Val Glu Pro 210 215

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Val Ile Gln Arg Gly His Glu Ser Leu Val His His Ile Leu Leu Tyr 230 -Gln Cys Ser Asn Asn Phe Asn Asp Ser Val Pro Gly Ile Arg Ala Arg 245 250 255 Ile Ala Ile Thr Pro Thr Cys Pro Net His Ser Ser Pro Val Lys Leu 260 265 270

<210> 305

<211> 207 <212> PRT

<213> Homo sapiens

<400> 305

Thr Gly Thr Phe Trp Ser Pro Arg Ser Gln Arg Arg Gly Cys Cys Gly

1 5 10 15

Arg Arg Ala Pro Arg Pro Glu Ala Met Glu Asn Gly Ala Val Tyr Ser 20 25 30

Pro Thr Thr Glu Glu Asp Pro Gly Pro Ala Arg Gly Pro Arg Ser Gly 35 40 45

Leu Lys Gly Leu Gln Leu Leu Leu Ser Leu Leu Ala Phe Ile Cys Glu 65 70 75 80

Glu Val Val Ser Gln Cys Thr Leu Cys Gly Gly Leu Tyr Phe Phe Glu 85 90 95

Phe Val Ser Cys Ser Ala Phe Leu Leu Ser Leu Leu Ile Leu Ile Val 100  $\phantom{\bigg|}105\phantom{\bigg|}$ 

Tyr Cys Thr Pro Phe Tyr Glu Arg Val Asp Thr Thr Lys Val Lys Ser 115 120 125

Ser Asp Phe Tyr Ile Thr Leu Gly Thr Gly Cys Val Phe Leu Leu Ala 130  $$135\$ 

Ser Ile Ile Phe Val Ser Thr His Asp Arg Thr Ser Ala Glu Ile Ala 145 150 155 160

Ala Ile Val Phe Gly Phe Ile Ala Ser Phe Met Phe Leu Leu Asp Phe 165 170 175

Ile Thr Met Leu Tyr Glu Lys Arg Gln Glu Ser Gln Leu Arg Lys Pro 180  $^{\circ}$  , 185 190

Glu Asn Thr Thr Arg Ala Glu Ala Leu Thr Glu Pro Leu Asn Ala 195 200 205

<210> 306 <211> 135 <212> PRT <213> Homo sapiens <400> 306 Ala Ser Ala Pro Ar-1

Ala Ser Ala Pro Arg Val Met Arg Gly His Leu Ala Gly Phe Pro Ala  $\frac{1}{5}$  10 15

Leu Ser Gly Leu Ala Ser Val Cys Leu Trp Ala Thr Phe Ser Ala Gln 20 25 30

Leu Pro Gly Pro Val Ala Ala Thr Ser Trp Thr Pro Ala Pro Leu Gly  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Cys Ser Ala Ala Arg Ser Gly Pro Glu Lys Arg Leu Gly Thr Ala Ala 50  $\,$   $^{\circ}55$   $\,$  60

Pro Gly Ser Ala Ala Ser Leu Ala Gln Ala Gly Pro Gly Ala Pro Cys 65 70 75 80

Arg Val Leu Pro Val Asp Pro Ala Pro Ala Ala Leu Asn Val Arg Glu 85 90 95

Pro Gly Trp Leu Gly Gly Leu Phe Asp Gly Ala Leu Leu Gln Val Leu 100 105 110

Leu Asn Phe Leu Arg Lys Ser Thr Asp Val Leu Met Asp Thr Arg Glu 115 120 125

Ala Glu Ser Leu Glu Val Glu 130 135

<210> 307 <211> 188 <212> PRT

<212> PRT

<213> Homo sapiens

<400> 307

Asn Lys Leu His Ser Phe Pro Val Phe Leu Ser Gln Leu Leu Seu Asp 1 5 10 15

Arg Gln Leu Leu His Ala Pro Gln Thr Leu Pro Thr  $\mbox{\colored}$  Pro His Cys Gly 20 25 30

Gly Ser Ser Arg Pro Gly Pro Ser His Pro Pro Trp Leu Leu Ile Gln 35 40 45

Leu Pro Cys Val His Val Ala Leu Trp Gln Met Leu Arg Asp Phe Ser 50 55 60

Asp Ser Arg Ile Thr Pro Ser Thr Leu Thr Thr Gln ?ro Ala Ala Gln 65 70 75 80

Thr Ala Ala Pro Ala Lys Asp Gln Glu Ser Asp Ile Val Gly Glu 85 90 95

Gly Ile Leu Cys Asp Ile Ala Phe Leu Gln Glu Asp His Pro Leu Gly

PCT/US99/17130 WO 00/06698 205

100 105 Val Gly Gly Ala Ser Ala Pro Ser Ser Arg Arg Glu Leu Ser Arg Arg 115 120 125 120 Gly Val His Thr Cln Thr Leu Pro Glu Asp Cly Thr Lcu His Cly Thr 130 135 140 Pro Ser Ser Ser Phe Asp Cys Gly Ile Lys Tyr Ile Ile Ser Trp Pro 145 150 155 160 Leu Ala Pro Gly Cys Asp Leu Pro Ser Leu Glu Leu Ser Leu Val Cys 165 170 175 Lys Gly Val Ser Ser Cys Met Gly Phe  $\lambda$ la Ala Gly 180 185 <210> 308 <211> 78 <212> PRT <213> Homo sapiens <400> 308 Pro Gly Arg Pro Thr Arg Pro Thr Lys Asn Lys Val Cys Val Cys Leu 1 5 10 15 Gly Met Leu Phe Trp Ala Tyr Pro Ile Cys Val Phe Ile Asp Ser Leu  $20 \hspace{1cm} 25 \hspace{1cm} 30$ Ser Cys Gln Pro Cys Leu Trp Ser Thr Gly Ala Thr Ser His Phe Asn 35 40 45 Ser Pro Thr Thr Ser Pro Leu Phe Thr Leu Phe Met Pro Cys Ala Leu 50 60Ala Pro Asn Pro Phe Thr Gln Leu Gly Lys Leu Asp Asp Arg 65 70 75 <210> 309 <21i> 10 <212> PRT <213> Homo sapiens <400> 309 Pro Val Asp Leu Thr Lys Thr Arg Leu Gln
1 5 10 <210> 310 <211> 10 <212> PRT <213> Homo sapiens

<400> 310

Pro Thr Asp Val Leu Lys Ile Arg Met Gln
1 5 10

<210> 311 <211> 313 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (117) <223> Xaa equals any of the naturally occurring L-amino acids Met Thr Phe Gly Ser Thr Ile Ser Pro Thr Ser Thr His Ala Ser Pro 1 5 10 15 Ser Leu Gly Phe Cys Cys Ser Trp Leu Leu Glu Asp Leu Glu Glu Gln Gln 20 25 30 Leu Tyr Cys Ser Ala Phe Glu Glu Ala Ala Leu Thr Arg Arg Ile Cys  $35 \hspace{1cm} 40 \hspace{1cm} 45$ Asn Pro Thr Ser Cys Trp Leu Pro Leu Asp Met Glu Leu Leu His Arg 50 . 55 60 Gln Val Leu Ala Leu Gln Thr Gln Arg Val Leu Cly Met Trp Leu 65 70 75 80 Arg Arg Ala Trp Asp Thr Trp Val Ser Pro Arg Arg Val Ala Pro Gly 85 90 95 Ser Arg Cys Leu Leu Thr Ala Ser His Pro Cys Thr Glu Lys Arg Arg 100 105 110 Lys Ala Ser Ala Xaa Gln Arg Asn Leu Gly Tyr Pro Leu Ala Met Leu 115 120 125Cys Leu Leu Val Leu Thr Gly Leu Ser Val Leu Ile Val Ala Ile His 130 135 140 Ile Leu Glu Leu Leu Ile Asp Glu Ala Ala Met Pro Arg Gly Met Gln Gly Thr Ser Leu Gly Gin Val Ser Phe Ser Lys Leu Gly Ser Phe Gly 165 170 175 Ala Val Ile Gln Val Val Leu Ile Phe Tyr Leu Met Val Ser Ser Val 180 185 190 Val Gly Phe Tyr Ser Ser Pro Leu Phe Arg Ser Leu Arg Pro Arg Trp 195 . 200 . 205 His Asp Thr Ala Met Thr Gln Ile Ile Gly Asn Cys Val Cys Leu Leu 210 215 220 Val Leu Ser Ser Ala Leu Pro Val Phe Ser Arg Thr Leu Gly Leu Thr 225 230 235 240 Arg Phe Asp Leu Leu Gly Asp Phe Gly Arg Phe Asn Trp Leu Gly Asn 245 250 250

Phe Tyr Ile Val Phe Leu Tyr Asn Ala Ala Phe Ala Gly Leu Thr Thr 260 265 270

Leu Cys Leu Val Lys Thr Phe Thr Ala Ala Val Arg Ala Glu Leu Ile 275 280 285

Arg Ala Phe Gly Leu Asp Arg Leu Pro Leu Pro Val Ser Gly Phe Pro 290 295 300

Gln Ala Ser Arg Lys Thr Gln His Gln

<210> 312

<211> 92

<212> PRT <213> Homo sapiens

<400> 312

Leu Cys Val Cys Leu Val Tyr Leu Cys Met Tyr Gly Val Cys Leu Cys 1 5 10 15

Val Ile Val Cys Val Ser Gly Val Ser Leu Cys Leu Tyr Val Trp Gly 20 25 30

Val Scr Val Cys Asp Cys Val Ser Val Phe Met Cys Val Cys Leu Cys 35 40 45

Val Ile Phe Cys Val Tyr Gly Lys Pro Arg Thr Glu His Tyr His Ser 50 55 60

Pro His Leu Ala Lys Gln Lys Ala Phe Arg Glu Met Cys Gly Arg His 65 70 75 80

Asp Val Ser Ala Ala Gly Ile Phe Gln Ser Tyr Val 85 90

<21C> 313

<211> 207

<212> PRT

<213> Homo sapiens

<400> 313

Gly His Met Pro Tyr Gly Trp Leu Thr Glu Ile Arg Ala Val Tyr Pro 1 5 10 15

Ala Phe Asp Lys Asn Asn Pro Ser Asn Lys Leu Val Ser Thr Ser Asn 20 25 30

Thr Val Thr Ala Ala His Ile Lys Lys Phe Thr Phe Val Cys Met Ala 35 40 45

Leu Ser Leu Thr Leu Cys Phe Val Met Phe Trp Thr Pro Asn Val Ser 50 60

Glu Lys Ile Leu Ile Asp Ile Ile Gly Val Asp Phe Ala Phe Ala Glu 65 70 75 80

Leu Cys Val Val Pro Leu Arg Ile Phe Ser Phe Phe Pro Val Pro Val 85 90 95

Phe Val Leu Ala Pro Ser Ser Val Leu Arg Ile Ile Val Leu Ile Ala 115 120 125

Ser Leu Val Val Leu Pro Tyr Leu Gly Val His Gly Ala Thr Leu Gly 130 135 140

Val Gly Ser Leu Leu Ala Gly Phe Val.Gly Glu Ser Thr Net Val Ala 145 150 155 160

Ile Ala Ala Cys Tyr Val Tyr Arg Lys Gln Lys Lys Lys Met Glu Asn 165 170 170

Glu Ser Ala Thr Glu Gly Glu Asp Ser Ala Met Thr Asp Met Pro Pro 180 185 190

Thr Glu Glu Val Thr Asp IIe Val Glu Met Arg Glu Glu Asn Glu 195  $200\,$  205

<210> 314

<211> 114

<212> PRT

<213> Homo sapiens

<400> 314

Gln Val Val Phe Val Ala Ile Leu Leu His Ser His Leu Glu Cys Arg 1 5 10 15

Glu Pro Leu Leu Ile Pro Ile Leu Ser Leu Tyr Met Gly Ala Leu Val 20  $$25\ \mbox{30}$$ 

Arg Cys Thr Thr Leu Cys Leu Gly Tyr Tyr Lys Asn Ile His Asp Ile  $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$ 

Ile Pro Asp Arg Ser Gly Pro Glu Leu Gly Gly Asp Ala Thr Ile Arg 50 55 60

Lys Met Leu Ser Phe Trp Trp Pro Leu Ala Leu Ile Leu Ala Thr Gln 65 70 75 80

Arg Ile Ser Arg Pro Ile Val Asn Leu Phe Val Ser Arg Asp Leu Gly 85 90 95

Gly Ser Ser Ala Ala Thr Glu Ala Val Ala Ile Leu Thr Ala Thr Tyr 100 105 110

Pro Val

<210> 315 <211> 115

PCT/US99/17130

209

<212> PRT

<213> Homo sapiens

<400> 315

Arg Cys Cys Cys Arg Gly Cys Ser Cys Arg Ala Arg Leu Cys Pro Pro 1 5 10 15

Ala Arg Ser Thr Ala Val Ala Pro Glu Cys Arg Gly Ala His Pro Ser 20 25 30

Arg Ala Met Arg Pro Gly Thr Ala Leu Gln Ala Val Leu Leu Ala Val 35 40 45

Leu Leu Val Gly Leu Arg Ala Ala Thr Gly Arg Leu Leu Ser Gly Gln 50 60

Pro Val Cys Arg Gly Gly Thr Gln Arg Pro Cys Tyr Lys Val Ile Tyr 65 70 75 80

Phe His Asp Thr Ser Arg Arg Leu Asn Phe Glu Glu Ala Lys Glu Ala 85 90 95.

Cys Arg Arg Gly Trp Arg Pro Ala Ser Gln His Arg Val Leu Lys Met 100 . 105 110

Asn Arg Asn 115

<210> 316 <211> 81

<212> PRT

<213> Homo sapiens

Met Arg Pro Gly Thr Ala Leu Gln Ala Val Leu Leu Ala Val Leu Leu 1 5 10 15

Val Gly Leu Arg Ala Ala Thr Gly Arg Leu Leu Ser Gly Gln Pro Val 20 25 30

Cys Arg Gly Gly Thr Gln Arg Pro Cys Tyr Lys Val Ile Tyr Phe His  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Asp Thr Ser Arg Arg Leu Asn Phe Glu Glu Ala Lys Glu Ala Cys Arg 50  $\,$  55  $\,$  60

Arg Gly Trp Arg Pro Ala Ser Gln His Arg Val Leu Lys Met Asn Arg 65 70 75 80

<210> 317 <211> 290 <212> PRT

<213> Homo sapiens

<400> 317 Ile Arg His Glu Gln Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro 1 5 10 15 Leu Ala Glu Ser Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro 20 25 30Asp Phe Thr Val Gln Ser His Arg Arg Ser Thr Val Asp Ser Ala Glu  $_{\mbox{\sc 35}}$ Asp Val His Ser Leu Asp Ser Cys Glu Tyr Ile Trp Glu Ala Gly Val 50 60Gly Phe Ala His Ser Pro Gln Pro Asn Tyr Ile His Asp Met Asn Arg 65 70 75 80 Met Glu Leu Leu Lys Leu Leu Leu Thr Cys Phe Ser Glu Ala Met Tyr 85 90 90 Leu Pro Pro Ala Pro Glu Ser Gly Ser Thr Asn Pro Trp Val Gln Phe Phe Cys Ser Thr Glu Asn Arg His Ala Leu Pro Leu Phe Thr Ser Leu 115 120 125 Leu Asn Thr Val Cys Ala Tyr Asp Pro Val Gly Tyr Gly Ile Pro Tyr 130 135 140 Asn His Leu Leu Phe Ser Asp Tyr Arg Glu Pro Leu Val Glu Glu Ala 145 150 155 160 Ala Gln Val Leu Ile Val Thr Leu Asp His Asp Ser Ala Ser Ser Ala 165  $\phantom{\bigg|}$  170  $\phantom{\bigg|}$  175 Ser Pro Thr Val Asp Gly Thr Thr Thr Gly Thr Ala Met Asp Asp Ala 180 185 190 Asp Pro Pro Gly Pro Glu Asn Leu Phe Val Asr Tyr Leu Ser Arg Ile 195 200 205 His Arg Glu Glu Asp Phe Gln Phe Ile Leu Lys Gly Ile Ala Arg Leu 210 215 220 Leu Ser Asn Pro Leu Leu Gln Thr Tyr Leu Pro Asn Ser Thr Lys Lys 225 230 235 240

Asp Pro Val Pro Pro Gly Ala Ala Ser Ser Leu Leu Glu Ala Leu Arg 245 250 255

Leu Gln Gln Glu Ile Pro Leu Leu Arg Ala Glu Glu Gln Arg Arg Pro 260 260 270

Arg His Pro Cys Pro His Pro Leu Leu Pro Gln Arg Cys Pro Gly Arg 275 280 285

Ser Val 290 <210> 318 <211> 318

<212> PRT

<213> Homo sapiens

<400> 318

Arg Leu Val Tyr Asn Lys Thr Ser Arg Ala Thr Gln Phe Pro Asp Gly
1 10 15

Val Asp Val Arg Val Pro Gly Phe Gly Lys Thr Phe Ser Leu Glu Phe 20 25 30

Leu Asp Pro Ser Lys Ser Ser Val Gly Ser Tyr Phe His Thr Met Val 35 40 45

Glu Ser Leu Val Gly Trp Gly Tyr Thr Arg Gly Glu App Val Arg Gly 50  $$^{55}$$ 

Ala Pro Tyr Asp Trp Arg Arg Ala Pro Asn Glu Asn Gly Pro Tyr Phe 65 70 75 80

Leu Ala Leu Arg Glu Met Ile Glu Glu Met Tyr Gln Leu Tyr Gly Gly 85 90 95

Pro Val Val Leu Val Ala His Ser Met Gly Asn Met Tyr Thr Leu Tyr 100 105 110

Phe Leu Gln Arg Gln Pro Gln Ala Trp Lys Asp Lys Tyr Ile Arg Ala 115 120 125

Phe Val Ser Leu Gly Ala Pro Trp Gly Gly Val Ala Lys Thr Leu Arg 130 135 140

Val Leu Ala Ser Gly Asp Asn Asn Arg Ile Pro Val Ile Gly Pro Leu 145 150 155 160

Lys Ile Arg Glu Gln Gln Arg Ser Ala Val Ser Thr Ser Trp Leu Leu 165 170 175

Pro Tyr Asn Tyr Thr Trp Ser Pro Glu Lys Val Phe Val Gln Thr Pro 180 195 190

Thr Ile Asn Tyr Thr Leu Arg Asp Tyr Arg Lys Phe Phe Gln Asp Ile 195 200 205

Gly Phe Glu Asp Cly Trp Leu Net Arg Gln Asp Thr Glu Gly Leu Val 210 215 220

Glu Ala Thr Met Pro Pro Gly Val Gln Leu His Cys Leu Tyr Gly Thr 225 230 235 . 240

Asp Pro Lys Ile Cys Phe Gly Asp Gly Asp Gly Thr Val Asn Leu Lys 260 265 270

Ser Ala Leu Gln Cys Gln Ala Trp Gln Ser Arg Gln Glu His Gln Val 275 280 285 PCT/US99/17130

Leu Leu Gln Glu Leu Pro Gly Ser Glu His Ile Glu Met Leu Ala Asn 290 295 300

Ala Thr Thr Leu Ala Tyr Leu Lys Arg Val Leu Leu Gly Pro 305 310 315

<210> 319

<211> 362

<212> PRT

<213> Homo sapiens

<400> 319

Met Asn Lys Glu Asp Lys Val Trp Asn Asp Cys Lys Gly Val Asn Lys 1 5 10 15

Leu Thr Asn Leu Glu Glu Gln Tyr Ile Ile Leu Ile Phe Gln Asn Gly 20 25 30

Leu Asp Pro Pro Ala Asn Met Val Phe Glu Ser Ile Ile Asn Glu Ile 35 40 45

Gly Ile Lys Asn Asn Ile Ser Asn Phe Phe Ala Lys Ile Pro Phe Glu 50 55 60

Glu Ala Asn Gly Arg Leu Val Ala Cys Thr Arg Thr Tyr Glu Glu Ser 65 70 75 80

Ile Lys Gly Ser Cys Gly Gln Lys Glu Asn Lys Ile Lys Thr Val Ser 85 90 95

Phe Glu Ser Lys Ile Gln Leu Arg Ser Lys Glr Glu Phe Gln Phe Phe 100 105 110

Asp Glu Glu Glu Glu Thr Gly Glu Asn His Thr Ile Phe Ile Gly Pro 115 120 125

Val Glu Lys Leu Ile Val Tyr Pro Pro Pro Pro Ala Lys Gly Gly Ile 130 135 140

Ser Val Thr Asn Glu Asp Leu His Cys Leu Asn Glu Gly Glu Phe Leu 145 150 155 160

Asn Asp Val Ile Ile Asp Phe Tyr Leu Lys Tyr Leu Val Leu Glu Lys 165 170 170 175

Leu Lys Lys Glu Asp Ala Asp Arg Ile His Ile Phe Ser Ser Phe Phe 180 185

Tyr Lys Arg Leu Asn Cln Arg Glu Arg Arg Asn His Glu Thr Thr Asn 195 200 205

Leu Ser Ile Gln Gln Lys Arg His Gly Arg Val Lys Thr Trp Thr Arg 210 215 220

His Val Asp Ile Phe Glu Lys Asp Phe Ile Phe Val Pro Leu Asn Glu 225 230 235 240

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Pro Lys Tyr Glu Pro Asn Pro His Tyr His Glu Asn Ala Val Ile Gln 260 265 270

Lys Cys Ser Thr Val Glu Asp Ser Cys Ile Ser Ser Ser Ala Ser Glu 275 280 285

Met Glu Ser Cys Ser Gln Asn Ser Ser Ala Lys Pro Val Ile Lys Lys 290 295 300

Met Leu Asn Lys Lys His Cys Ile Ala Val Ile Asp Ser Asn Pro Gly 305 310 315 320

Gln Glu Glu Ser Asp Pro Arg Tyr Lys Arg Asn Ile Cys Ser Val Lys 325  $\frac{1}{2}$  330 335

Tyr Ser Val Lys Lys 11e Asn His Thr Ala Ser Glu Asn Glu Glu Phe 340 350

Asn Lys Gly Glu Ser Thr Scr Gln Lys Ser

<210> 320

<211> 330

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (38)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (247)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 320

Met Ser Pro Leu Ser Ala Ala Arg Ala Ala Leu Arg Val Tyr Ala Val 1 5 10 15

Gly Ala Ala Val Ile Leu Ala Gin Leu Leu Arg Arg Cys Arg Gly Gly . 20 25 30

Phe Leu Glu Pro Val Xaa Pro Pro Arg Pro Asp Arg Val Ala Ile Val 35

Thr Gly Gly Thr Asp Gly Ile Gly Tyr Ser Thr Ala Asn Ile Trp Arg
50 55 60

Asp Leu Gly Met His Val Ile Ile Ala Gly Asn Asn Asp Ser Lys Ala 65 70 75 80

Lys Gln Val Val Ser Lys Ile Lys Glu Glu Thr Leu Asn Asp Lys Val 85 90 95

Glu Phe Leu Tyr Cys Asp Leu Ala Ser Me: Thr Ser Ile Arg Gln Phe 100 105 110 Val Gln Lys Phe Lys Met Lys Lys Ile Pro Leu His Val Leu Ile Asn 115 120 125 Asn Ala Gly Val Met Met Val Pro Gln Arg Lys Thr Arg Asp Gly Phe 130 140 Glu Glu His Phe Gly Leu Asn Tyr Leu Gly His Phe Leu Leu Thr Asn 145 150 155 160 Leu Leu Leu Asp Thr Leu Lys Glu Ser Gly Ser Pro Gly His Ser Ala 165 . 170 . 175 Arg Val Val Thr Val Ser Ser Ala Thr His Tyr Val Ala Glu Leu Asn 180 185 190 Met Asp Asp Leu Gln Ser Ser Ala Cys Tyr Ser Pro His Ala Ala Tyr 195 200 205 Ala Gln Ser Lys Leu Ala Leu Val Leu Phe Thr Tyr His Leu Gln Arg 210 215 220 Leu Leu Ala Ala Glu Gly Ser His Val Thr Ala Asn Val Val Asp Pro 225 230 235 240 Leu Ala Lys Lys Leu Leu Gly Trp Leu Leu Phe Lys Thr Pro Asp Glu 260 265 270 Gly Ala Trp Thr Ser Ile Tyr Ala Ala Val Thr Pro Glu Leu Glu Gly 275 280 . 285 Val Gly Gly Arg Tyr Leu Tyr Asn Glu Lys Glu Thr Lys Ser Leu His 290 295 300 Val Thr Tyr Asn Gln Lys Leu Gln Gln Gln Leu Trp Ser Lys Ser Cys 305 310 315 320 Glu Met Thr Gly Val Leu Asp Val Thr Leu 325 330 <210> 321 <211> 71 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (38) <223> Xaa equals any of the naturally occurring L-amino acids

Met Ser Pro Leu Ser Ala Ala Arg Ala Ala Leu Arg Val Tyr Ala Val 1 5 10 15

<400> 321

```
Gly Ala Ala Val 11e Let Ala Gln Let Let Arg Arg Cys Arg Cly Gly 20 25 30

Phe Let Glt Pro Val Xaa Pro Pro Arg Pro Asp Arg Val Ala 11e Val 35 40 Thr Gly Gly Thr Asp Gly Ile Gly Tyr Ser Thr Ala Asn Ile Trp Arg
```

Asp Leu Ala Cys Met Leu Ser

```
<210> 322
<211> 266
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (97)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (174)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (195)
<223> Xaa equals any of the naturally occurring L-amino acids
<220>
<221> SITE
<222> (199)
<223> Xaa equals any of the naturally occurring L-amino acids
<221> SITE
<222> (206)
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<400> 322
Met Glu Val Thr Thr Glu Asp Thr Ser Arg Thr Asp Val Ser Clu Pro
1

<223> Xaa equals any of the naturally occurring L-amino acids

Ala Thr Ser Gly Gly Ala Ala Asp Gly Val Thr Ser Ile Ala Pro Thr

Ala Val Ala Ser Ser Thr Thr Ala Ala Ser Ile Thr Thr Ala Ala Ser
35 40 45

Ser Net Thr Val Ala Ser Ser Ala Pro Thr Thr Ala Ala Ser Ser Thr 50 55 60

Thr Val Ala Ser Ile Ala Pro Thr Thr Thr Ala Ser Ser Met Thr Ala 65 70 75 80

> Ala Ser Ser Thr Pro Met Thr Leu Ala Leu Pro Ala Pro Thr Ser Thr Xaa Thr Gly Arg Thr Pro Ser Thr Thr Ala Thr Gly His Pro Ser Leu Ser Thr Ala Leu Ala Gln Val Pro Lys Ser Ser Ala Leu Pro Arg Thr Ala Thr Leu Ala Thr Leu Ala Thr Arg Ala Gln Thr Val Ala Thr Thr 130  $$135\$ Ala Asn Thr Ser Ser Pro Met Ser Thr Arg Pro Ser Pro Ser Lys His 145 155 160 Mot Pro Ser Asp Thr Ala Ala Ser Pro Val Pro Pro Met Xaa Pro Gln 165 170 170 Ala Gln Gly Pro Ile Ser Gln Val Ser Val Asp Gln Pro Val Val Asn 180 190 Leu Thr Gln Ala Val Val Asp Lys Thr Leu Leu Leu Val Val Leu Leu 210 215 Leu Gly Val Thr Leu Phe Ile Thr Val Leu Val Leu Phe Ala Leu Gln 225 230 240 Ala Tyr Glu Ser Tyr Lys Lys Lys Asp Tyr Thr Gln Val Asp Tyr Leu 245 250 255 Ile Asn Gly Met Tyr Ala Asp Ser Glu Met 260 265

<210> 323 <211> 99

<212> PRT

<213> Homo sapiens

Ala Arg Cys Pro Glu Leu Pro Gly Leu Arg Cys Arg Pro Arg Pro Arg 1 5 10 15

Ala Gly Pro Gln Ala Pro Ser Tyr Cys Pro Arg Ala Thr Arg Pro Pro 20 . 25 30

Gly Ala Cys Cys Ala Arg Met Arg Leu Leu Ceu Glu Trp Arg Val Tyr 35 40 45

Leu Arg Leu Thr Cys Ala Thr Lys Asp Gly Met Ala Arg Glu Cys Pro  $50 \hspace{1cm} 55$ 

Thr Thr Trp Leu Ser Pro Pro Ala Lys Pro Asp Phe Ala Gln Arg His 65 70 75 80

217

Ser Val Lys Pro Thr Ala Leu Gin Gly Gly Arg Trp Ser Arg Leu Gly

Ala Ser Pro

<210> 324

<211> 96

<212> PRT

<213> Homo sapiens

<400> 324

Leu Pro Ala Thr Val Glu Phe Ala Val His Thr Phe Asn Gln Gln Ser

Lys Asp Tyr Tyr Ala  $_{0}$ Tyr Arg Leu Gly His Ile Leu Asn Ser Trp Lys 20 25 30

Glu Gln Val Glu Ser Lys Thr Val Phe Ser Met Glu Leu Leu Gly 40

Arg Thr Arg Cys Gly Lys Phe Glu Asp Asp Ile Asp Asr Cys His Phe 50 60

Gln Glu Ser Thr Glu Leu Asn Asn Thr Phe Thr Cys Phe Phe Thr Ile 65 70 75 80

Ser Thr Arg Pro Trp Met Thr Gln Phe Ser Leu Leu Asn Lys Thr Cys  $85 \hspace{0.5cm} 90 \hspace{0.5cm} 95 \hspace{0.5cm} 95 \hspace{0.5cm}$ 

<210> 325

<211> 166 <212> PRT

<213> Homo sapiens

<400> 325

Leu Leu Trp Ala Arg Gly Leu Gly Arg Ala Lys Ser Ala Val Pro Thr  $\frac{1}{5}$  10 15

Val Ser Thr Met Leu Gly Leu Pro Trp Lys Gly Gly Leu Ser Trp Ala 20 25 30

Leu Leu Leu Leu Leu Gly Ser Gln ile Leu Leu Ile Tyr Ala Trp 35 40 45

His Phe His Glu Gln Arg Asp Cys Asp Glu His Asn Val Met Ala Arg 50 55 60

Tyr Leu Pro Ala Thr Val Glu Phe Ala Val His Thr Phe Asn Gln Gln 65 70 75 80

Ser Lys Asp Tyr Tyr Ala Tyr Arg Leu Gly His Ile Leu Asa Ser Trp 85 90 95

218

Lys Glu Gin Val Glu Ser Lys Thr Val Phe Ser Met Glu Leu Leu Leu 100 . 105 . 110

Gly Arg Thr Arg Cys Gly Lys Phe Glu Asp Asp Ile Asp Asn Cys His 115 120 125

Phe Gln Glu Ser Thr Glu Leu Asn Asn Thr Phe Thr Cys Phe Phe Thr 130 135 140

Cys Leu Glu Gly Phe His

<210> 326

<211> 214

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (200)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (205)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 326

Leu Glu Gln Lys Leu Glu Leu His Arg Gly Gly Gly Arg Ser Arg Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Ser Gly Ser Pro Gly Leu Cln Glu Pne Gly Thr Arg Glu Glu Arg Gly 20  $\phantom{-}25\phantom{+}30\phantom{+}$ 

Glu Gly Glu Gln Arg Thr Gly Arg Glu Phe Ser Gly Asn Gly Gly Arg 35 40 45

Ala Val Glu Ala Ala Arg Met Arg Leu Leu Cys Gly Leu Trp Leu Trp 50 55 60 .

Leu Ser Leu Leu Lys Val Leu Gln Ala Gln Thr Pro Thr Pro Leu Pro 65 70 75 80

Leu Pro Pro Pro Met Gln Ser Phe Gln Gly Asn Gln Phe Gln Gly Glu 85 90 95

Trp Phe Val Leu Gly Leu Ala Gly Asr. Ser Phe Arg Pro Glu His Arg 100 105 110

Ala Leu Leu Asn Ala Phe Thr Ala Thr Phe Glu Leu Ser Asp Asp Gly 115 120 125

Arg Phe Glu Val Trp Asn Ala Met Tar Arg Gly Gln His Cys Asp Thr 130 135 140 Trp Ser Tyr Val Leu Ile Pro Ala Ala Gln Pro Gly Gln Phe Thr Val 145 150 155 160

Asp His Gly Val Gly Arg Ser Trp Leu Leu Pro Pro Gly Thr Leu Asp 165 170 170

Gln Phe Ile Cys Leu Gly Arg Ala Gln Gly Leu Ser Asp Asn Ile 180 185 190

Val Phe Pro Asp Val Thr Gly Xaa Ala Leu Asp Leu Xaa Ser Leu Pro 195 200 205

Trp Val Ala Ala Pro Ala 210

<210> 327 <211> 181

<212> PRT

<213> Homo sapiens

Met Cys Val Cys Glu Arg Lys Arg Gly Arg Glu Lys Glu Gly Gly Val

Thr Pro Thr Met Thr Ser Asn Phe Pro Phe Cys Thr Leu Ile Leu Gly 20 25 30

The Ala Gln Ala Gln Ala Cys Pro Gly Cys Pro Gly Asp Trp Pro Gly  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Leu Gly Ser Gly Val Gly Glu Gly Leu His His Ile Arg Thr Cys Arg 50 60

Thr Pro Ile Pro Cys Ser Pro Pro Ala Pro Ala Ala Ala Cys Leu Gly 65 70 75 80

Ser Cly His Ala Arg Leu Pro Cys Val Leu Arg Leu Trp Pro Val Pro 85 90 95

Ala Asn Leu Ser Ser Pro Phe Arg Leu Glu Ala Leu His Cys Ser Phe 100 105 110

Trp Ser Ser Pro Leu Leu Pro Ala Pro His Leu Ala Phe Phe Gly Phe 115 120 125

Arg Asp Leu Leu Thr Asp Phe Leu Leu Ala Ala Cys Leu Leu Thr Phe 130 135 140

Gln Lys Thr Pro Leu Glu Leu Pro Met Ala Val Val His Leu Leu Val 145 150 150 155

Ala Thr Pro Cys Tyr Gin Net Leu Asp Asn Leu Pro Leu Pro Ser Ala 165 170 175

Ala Ala Asn Trp Cys 180

<210> 328 <211> 195 <212> PRT

<213> Homo sapiens

<400> 32B

Tyr Leu Trp Gly Arg Pro Arg Leu Arg Met Arg Ala Gly Thr Ser Pro 1 5 10 15

Ser Ala Pro Trp Gly Glu Lys Arg Glu Lys Leu Gly His Lys Leu Pro  $20 \\ 25 \\ 30$ 

Val Ala Leu Gln Gly Tyr His Pro Trp Ile Leu Leu Glu Cys Thr Val 35 40 . 45

Phe Trp Ala Arg Val Val Leu Ala Cys Phe Ser Leu Tyr Leu Ile Arg 50  $\checkmark 55$  60

Gly Pro Asn Cys Ile Asn Arg Gln Pro Glu Pro Thr Tyr Gln Lys Ala 65 70 75 80

Cys Asn Leu Asp Cys Scr Ser Asp Phe Gly Gln Glu Arg Ala Pro Ala 85 90 95

Trp Glu Leu Leu Gly Pro Glu Ser Glu Gln Arg Leu Arg Glu Tyr Thr

Ala Gln Gly Leu Gln Ser Leu Ala Ser Ser His Arg Trp Arg Gln Phe 115 120 125

Lys Thr Glu Gly Lys Met Arg Gly Gly Ala Ser Pro Leu Pro Trp Leu 130 135 140

Ile Cys Phe Trp Leu Cys Ser Tyr Lys Gly Ser Asp Asn Ser Leu Lys 145 150 155 160

Pro Val Val Pro Gly Pro Thr Leu Cys Pro Gln Ser Leu Val Ser Pro 165 170 175

Ser Val His Pro Ser Thr Arg Ser Ala Ser Leu Gly Arg His Arg Ala 180 185 190

Glu Ala Ala

<210> 329

<211> 50

<212> PRT

<213> Homo sapiers

<400> 329

Met Pro Gly Ile Leu Ala Gly Ile Pro Val Lys Asp Leu Cys Leu Ser

Leu Leu Gln Gly Phe Arg Leu Leu Leu Leu Cys Val Cys Pro Gly Trp
20 . 25 . 30

Leu Ser Gly Trp Met Gly Gly Gln Lys Gly Ser Pro Arg Ile Val Asp

```
35
                                     40
                                                             45
 Ile Gly
 <210> 330
 <211> 90
 <212> PRT
 <213> Homo sapiens
 <400> 330
Ala Lys Gly Glu Glu Arg Lys Glu Ala Phe Ser Leu Lys Met Val Gln ^{1} 5 . 10 . 15
Leu Ser Ser Glu Pro Ile Ser Phe Gly Leu Met Tyr Leu Tyr Leu Gly 20 \pm 25 30
Val Phe Phe His Leu Ile Tyr Pro Gly Ala Leu Ser Ile Thr Thr Leu 35 \hspace{1.5cm} 40 \hspace{1.5cm} 45
Cly Lys His Ser His Pro Phe Phe Thr Ala Glu Gln Asa Ser Thr Val 50 55 60
Trp Met Glu His Thr Leu Phe His Gln Ser Pro Val Ala Ser His Leu 65 70 75 80
Val Cys Phe Gln Ser Phe Ala Phe Ser Glu
85 90
<210> 331
<211> 56
<212> PRT
<213> Homo sapiers
<400> 331
Gly Pro Ala His Pro Ala Ser Pro Pro Leu Met Thr Leu Ser Leu Gln
1 5 10 15
Leu Ala Glu Leu Val His Phe Val Cys Ala Phe Gln Ser Gln Trp Thr 20 25 30
Gly Val Tyr ?ro Met Met Pro Pro Leu Lys Pro Thr Glu Pro Leu Cys 35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}
Phe Ala Cys Val Pro Cys Arg Val
<210> 332
<211> 18
<212> PRT
<213> Homo sapiens
<400> 332
Met Leu Leu Glu Val Tyr Gly Asp Ser Ile Ser Val Thr Val Ala Ile
1 5 10 15
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Pro Leu
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<210> 333

<211> 19

<212> PRT <213> Homo sapiens

<400> 333

Met His Ser Pro Cys Gln Ser Lys Ala Ala Asp Gly Leu Gly Lys Ser 1 5 10 15

Glu Thr Glu

<210> 334

<211> 10 <212> PRT

<213> Homo sapiens

<400> 334

Met Leu Lys Ser Leu Gly Leu Ser Thr Asn 1 5 10

<210> 335 <211> 200 <212> PRT

<213> Homo sapiens

Ala Gln Arg Leu Ala Glu Glu Cys Phe Tyr Met Leu Leu Glu Val Tyr

1 5 10 15

Cys Gln Ser Lys Ala Ala Asp Gly Leu Gly Lys Ser Glu Thr Glu Met  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Leu Lys Ser Leu Gly Leu Ser Thr Asn Net Ser Pro Phe His Leu Leu 50 60

Gly Leu Lys Val Phe Leu Thr Trp Ala Leu Thr Leu Ala Gln Ile Cys 65 70 75 80

Leu Tyr Phe Phe Glu Val Gln Pro Leu Gly Leu Leu Ala Leu Asn Phe  $85 \hspace{1cm} 90 \hspace{1cm} 95$ 

Phe Cys Thr Ala Thr Ala Gly Leu Lys Glu Leu Cys Met His Pro Pro 100 105 110

Ser Leu Ala Phe Thr Pro Glu Phe His Thr Ser Leu Ser Pro Leu Ala 115 120 125

Ile Pro Ser Phe Cys Gly Thr Ser Val Ser Leu Ser Asn Ser His Thr 130 135 140

Tle Pro Leu Ser Leu Tyr Leu Pro Phe Pro Ser Lys Ser Arg Met Pro 145 150 155 160

Asp Thr Leu His Leu Leu Val His Ser Leu Pro Leu Val His Ser Gln 165 170 175

Val Leu Pro Val Lys Asp Val Thr Ile Glu Trp Pro Leu Cys Gln Arg 180 185 190

Cys Leu Gly Ser Thr Cys His Gln 195 200

<210> 336

<211> 99

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (94)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (99)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 336

Trp Ile Pro Arg Ala Ala Gly Ile Arg His Glu Val Gln Val Ser Leu 1 5 10 15

Phe Gln Met Phe Cys Phe Ser Ser Ile Phe Cys Ser His Glu His Thr

His Leu Pro Gly Thr Phe Trp Leu Pho Leu Phe Leu Phe Leu Ile Leu 35 . 40 . 45

Pro Pro Ser Cys Pro Cys Phe Leu Pro Phe Ser Leu Ala Ile Glu Thr 50 55 60

Val Arg Trp Pro Cys Trp His His Pro Thr Ser Phe Glu Leu Cys Tyr 65 70 75 80

Pro Gly Thr Ser Ile Tyr Tyr Ala Ser Arg Gly Gly Pro Xaa Pro Asn 85 90 95

Ser Glu Xaa

<210> 337

<211> 96 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<210> 338

Pro Arg Val Arg Lys Glu Pro Glu Ala Met Gln Trp Leu Arg Val Arg

Glu Ser Pro Gly Glu Ala Thr Gly His Arg Val Thr Met Gly Thr Ala  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Ala Leu Gly ?ro Val Trp Ala Ala Leu Leu Leu Phe Leu Leu Met Cys 35 40 45

Glu Ile Pro Met Val Glu Leu Thr Phe Asp Arg Ala Val Ala Ser Asp  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Cys Gln Arg Cys Cys Asp Ser Glu Asp Pro Leu Asp Pro Ala His Val 65 70 75 80

Ser Ser Ala Ser Ser Ser Gly Arg Pro His Ala Leu Pro Glu Ile Arg 85 90 95

Pro Tyr Iie Asn Ile Thr Ile Leu Lys Gly Asp Lys Gly Asp Pro Gly 100 - 105 110

Pro Met Gly Leu Pro Gly Tyr Met Gly Arg Glu Gly Pro Gln Gly Glu 115 120 125

Pro Gly Pro Gln Gly Ser Lys Gly Asp Lys Gly Glu Met Gly Ser Pro 130 135 140

Gly Ala Pro Cys Gln Lys Arg Phe Phe Ala Phe Ser Val Gly Arg Lys 145 150 155 160

Thr Ala Leu His Ser Gly Glu Asp Phe Gln Thr Leu Leu Phe Glu Arg 165 170 175

Val Phe Val Asn Leu Asp Gly Cys Phe Asp Met Ala Thr Gly Gln Phe 180 185 190

Ala Ala Pro Leu Arg Gly Ile Tyr Phe Phe Ser Leu Asn Val His Ser 195 200 205

Trp Asn Tyr Lys Glu Thr Tyr Val His Ile Met His Asn Gln Lys Glu 210 215 220

Ala Val Ile Leu Tyr Ala Gln Pro Ser Glu Arg Ser Ile Met Gln Ser 225 230 235 240

Leu Phe Lys Arg Gln Arg Glu Asn Ala Ile Tyr Ser Asn Asp Pho Asp 260 265 270

Thr Tyr Ile Thr Phe Ser Gly His Leu Ile Lys Ala Glu Asp Asp 275 280 285

<210> 340

<211> 339

<212> PRT

<213> Homo sapiens

<400> 340

Met Leu Tyr Pro Gly Ser Val Tyr Leu Leu Glr. Lys Ala Leu Met Pro

1	•			,	•				10	)				15	<b>5</b> .
Val	. Le	Leu	Gln 20	Gly	Gln	Ala	a Arg	, Lev 25	ı Val	l Glu	ı Glı	ι Сγε	Asr 30		/ Arg
Arg	Ala	Lys 35	Leu	Leu	Ala	Суя	Asp 40	Gly	/ Asr	: Glu	ı Ile	Asp 45		Met	Phe
Val	Asp 50	Arg	Arg	Gly	Thr	A1a 55	Glu S	Pro	Glr	Gly	Glr 60		Leu	Va]	. Ile
65					Ala 70					75					80
				85		<u>.</u>			90					95	
			100		Val			105					110		-
		115			Phe		120					125			
	130				Ala	135					140				
145					Pro 150					155				٠	160
				165	Pro				170					175	
			180		Arg			185					190		
		195			Arg		200					205			
	210				lle	215					220				
425					Leu 230					235					240
				245	Glu				250					255	
			260		GLu			265					270		
		275			Leu		280	٠				285			
	290					295					300				
05	Arg	Gln	Leu	Ala	Leu 310	Phe	Leu	Ala	Arg	Lys 315	His	Leu	His	Asn	Phe 320

227

Glu Ala Thr His Cys Thr Pro Leu Pro Ala Gln Asn Phe Gln Met Pro 325 330 335

Trp His Leu

<210> 341

<211> 127

<212> PRT

<213> Homo sapiens

<400> 341

Val Cys Pro Lys Trp Cys Arg Phe Leu Thr Met Leu Gly His Cys Cys

1 10 15

Tyr Phe Trp Gln Val Trp Pro Ala Scr Glu Ala Leu Ala Ala Gly Pro 20 25 30

Thr Pro Ser Thr Gly Ser Ser Ser Pro Ser Trp Lys Gln His Ile Gly 35 40 45

Thr Ser Leu Gln Lys Thr Arg Gly Ser Leu Pro Thr Thr Thr Leu Thr 50 55 60

Ser Gly Ala Gly Gln Ser Thr Ser Thr Gly Lys Asn Pro Ala Ala Gly 65 70 75 80

Arg Ser Leu Glu Gly Ala Leu Pro Ala Gly Val Trp Pro Cys Phe Ala 85 90 95

Gln Ser Pro Cys Thr Gly Gly Gln Gln Thr Pro Ser Ser Thr Gly Leu 100 105 110

Arg Ser Cys Leu Val Arg Ser Pro Ala Thr Trp Trp Arg Thr Pro 115 120 125

<210> 342

<211> 554

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (16)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (109)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 342

Trp Ile Pro Arg Ala Ala Gly Ile Arg His Glu Ile Tyr Arg Clu Xaa 1 5 10 15

Asp Ser Glu Arg Ala Pro Ala Ser Val Pro Glu Thr Pro Thr Ala Val 20 25 30

Thr	· Ala	3 Pro	o His	s Ser	Ser	Ser	T∑₽ 40	) Asp	Th	тут	Тут	Glr 45		Arg	, Al
Leu	G10 50	ı Lys	s His	s Ala	Asp	Ser 55		Leu	Ala	Leu	Ala 60		· Val	Phe	Tr
Ser 65	Ile	e Sei	туг	туг	Ser 70		Pro	Phe	Ale	Phe 75		Туг	Leu	Туг	Ar 8
Lys	Gly	7 Туз	Lev	Ser 85	Leu	Ser	Lys	Val	Val 90		Phe	Ser	His	Туг 95	
Gly	Thr	Leu	100	Leu )	Leu	Leu	Ala	Gly 105		Ala	Cys	Xaa	Arg 110		11
Gly	Arg	115	Thr	Asn	Pro	·'Gln	Туг 120	Arg	Gln	Pho		Thr 125		Leu	G1
Ala	Thr 130	His	Arg	Asn	Gln	Ser 135	Ser	Glu	Asn	Lγs	Arg 140	Gln	Leu	Ala	As
Tyr 145	Asn	Phe	Asp	?he	Arg 150	Ser	Trp	Pro	Val	Asp 155	Phe	His	Trp	Glu	G1: 16
				165	Glu				170					175	
			180		Glu			185					190		
		195			Lys		200					205			
	210		•	٠	Arg	215					220				
225					Met 230					235					240
				245	Gly				250					255	
			260		Met			265					270		
Gln	Gly	Gln 275	Lys	Leu	Val	Ile	Суз 280	Суз	Glu	Gly	neA	Ala 285	Gly	Phe	туг
Glu	Val 290	GJĀ	СЛа	Val	Ser	Thr 295	Pro	Leu	Glu	Ala	Gly 300	Tyr	Ser	Val	Leu
Gly 305	Trp	Asn	His	Pro	Gly 310	Phe	Ala	Gly	Ser	Thr 315	Gly	Val	Pro	Phe	Pro 320
Gln	Asn	Glu	Ala	Asn 325	Ala	Met	qaA		Val 330	Val	Gln	Phe	Ala	Ile 335	His

Arg Leu Gly Phe Glr. Pro Gln Asp Ile Ile Ile Tyr Ale Trp Ser Ile

340 Gly Gly Phe Thr Ala Thr Trp Ala Ala Met Ser Tyr Pro Asp Val Ser Ala Net Ile Leu Asp Ala Ser Phe Asp Asp Leu Val Pro Leu Ala J.eu 370 380 Lys Val Met Pro Asp Ser Trp Arg Gly Leu Val Thr Arg Thr Val Arg 385 390 395 400 Gln His Leu Asn Leu Asn Asn Ala Glu Gln Leu Cys Arg Tyr Gln Gly
405 410 415 Pro Val Leu Leu Ile Arg Arg Thr Lys Asp Glu Ile Ile Thr Thr 420 425 430 Val Pro Glu Asp Ile Met Ser Asm Arg Gly Asm Asp Leu Leu Lys 435 440 445 Leu Leu Gln His Arg Tyr Pro Arg Val Met Ala Glu Glu Gly Leu Arg 450 460 Val Val Arg Gln Trp Leu Glu Ala Ser Ser Gln Leu Glu Glu Ala Ser 465 470 475 480 Ile Tyr Ser Arg Trp Glu Val Clu Clu Asp Trp Cys Leu Ser Val Leu
485 490 495 Arg Ser Tyr Gln Ala Glu His Gly Pro Asp Phe Pro Trp Ser Val Gly 500 505 510 Glu Asp Met Ser Ala Asp Gly Arg Arg Gln Leu Ala Leu Phe Leu Ala 515 520 525 Arg Lys His Leu His Asn Phe Glu Ala Thr His Cys Thr Pro Leu Pro 530 540 Ala Gln Asn Phe Gln Met Pro Trp His Leu 5**45** 550 <210> 343 <211> 225 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (5) <223> Xaa equals any of the naturally occurring L-amino acids His Glu Arg Ala Xaa Gly Pro Ser Arg Gly His Gly Glu Leu Leu Ser 1 5 10 15

Cys Val Leu Gly Pro Arg Leu Tyr Lys Ile Tyr Arg Glu Arg Asp Ser 20 25 30

Glu Arg Ala Pro Ala Ser Val Pro Glu Thr Pro Thr Ala Val Thr Ala 35 40 45

Pro His Ser Ser Ser Trp Asp Thr Tyr Tyr Gln Pro Arg Ala Leu Glu 50 55 60

Lys His Ala Asp Ser Ile Leu Ala Leu Ala Ser Val Phe Trp Ser Ile 65 70 75 80

Ser Tyr Tyr Ser Ser Pro Phe Ala Phe Phe Tyr Leu Tyr Arg Lys Gly
85 90 95

Tyr Leu Ser Leu Ser Lys Val Val Pro Phe Ser His Tyr Ala Gly Thr 100 105 110

Leu Leu Leu Leu Ala Gly Val Ala Cys Ser Glu Ala Leu Ala Ala 115 : 120 : 125

Gly Pro Thr Pro Ser Thr Gly Ser Ser Ser Pro Ser Trp Lys Gln His 130 . 135 140

Ile Gly Thr Ser Leu Gln Lys Thr Arg Gly Ser Leu Pro Chr Thr Thr 145 150 155 160

Leu Thr Ser Gly Ala Gly Gln Ser Thr Ser Thr Gly Lys Asn Pro Ala 165 170 175

Ala Cly Arg Ser Leu Glu Gly Ala Leu Pro Ala Gly Val Trp Pro Cys 180 185 190

Phe Ala Gln Ser Pro Cys Thr Gly Gly Gln Gln Thr Pro Ser Ser Thr 195 200 205

Gly Leu Arg Ser Cys Leu Val Arg Ser Pro Ala Thr Trp Trp Arg Chr 210 215 220

Pro 225

<210> 344

<211> 299

<212> PRT

<213> Homo sapiens

<400> 344

Met Phe Lys Arg. His Gln Arg Leu Lys Lys Asp Ser Thr Gln Ala Glu

1 5 10 15

Glu Asp Leu Ser Glu Gln Glu Gln Asn Gln Leu Asn Val Leu Lys Lys 20 25 30

His Gly Tyr Val Val Gly Arg Val Gly Arg Thr Phe Leu Tyr Ser Glu
35 40 45

Giu Gln Lys Asp Asn Ile Pro Phe Glu Phe Asp Ala Asp Ser Leu Ala 50 55 60

Phe Asp Met Glu Asn Asp Pro Val Met Gly Thr His Lys Ser Thr Lys

70

65

<222> (211)

WO 00/06698 PCT/US99/17130

Gln Val Glu Leu Thr Ala Gln Asp Val Lys Asp Ala His Trp Phe Tyr Asp Thr Pro Gly Ile Thr Lys Glu Asn Cys Ile Leu Asn Leu Thr 100 105 110 Glu Lys Glu Val Asn Ile Val Lcu Pro Thr Gln Ser Ile Val Pro Arg 115 120 125 Thr Phe Val Leu Lys Pro Gly Met Val Leu Phe Leu Gly Ala Ile Gly 130 135 140 Arg Ile Asp Phe Leu Gln Gly Asn Gln Ser Ala Trp Phe Thr Val Val 145 150 155 160 Ala Ser Asn Ile Leu Pro Val His Ile Thr Ser Leu Asp Arg Ala Asp 165 170 175 Ala Leu Tyr Gln Lys His Ala Gly His Thr Leu Leu Gln Ile Pro Met 180 185 190 Gly Gly Lys Glu Arg Met Ala Gly Phe Pro Pro Leu Val Ala Glu Asp 195 200 205 Ile Met Leu Lys Glu Cly Leu Cly Ala Ser Glu Ala Val Ala Asp Ile 210 215 220 Lys Phe Ser Ser Ala Gly Trp Val Ser Val Thr Pro Asn Phe Lys Asp 225 230 230 235 Arg Leu His Leu Arg Gly Tyr Thr Pro Glu Gly Thr Val Leu Thr Val 245  $\phantom{\bigg|}255\phantom{\bigg|}$ Arg Pro Pro Leu Leu Pro Tyr Ile Val Asn Ile Lys Gly Gln Arg Ile 260 265 270 Lys Lys Ser Val Ala Tyr Lys Thr Lys Lys Pro Pro Ser Leu Met Tyr 275 280 285 Asn Val Arg Lys Lys Lys Gly Lys Ile Asn Val 290 295 <210> 345 <211> 314 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (147) <223> Xaa equals any of the naturally occurring L-amino acids <220> <221> SITE

<223> Xaa equals any of the naturally occurring L-amino acids

Met Leu Pro Ala Arg Leu Pro Phe Arg Leu Leu Ser Leu Phe Leu Arg

1 5 10 15 Gly Ser Ala Pro Thr Ala Ala Arg His Gly Leu Arg Glu Pro Leu Leu 20 25 30 Glu Arg Arg Cys Ala Ala Ala Ser Ser Phe Gln His Ser Ser Ser Leu 35 40 45 Gly Arg Glu Leu Pro Tyr Asp Pro Val Asp Thr Glu Gly Phe Gly Glu 50 55 60Gly Gly Asp Met Gln Glu Arg Phe Leu Phe Pro Glu Tyr Ile Leu Asp 65 70 75 80 Pro Glu Pro Gln Pro Thr Arg Glu Lys Gln Leu Gln Glu Leu Gln Gln 85 90 95 Gln Glu Glu Glu Glu Arg Cln Arg Gln Gln Arg Arg Glu Glu Arg 100 105 110 Arg Gln Gln Asn Leu Arg Ala Arg Ser Arg Glu His Pro Val Val Gly 115 120 125His Pro Asp Pro Ala Leu Pro Pro Ser Gly Val Asn Cys Ser Gly Cys 130 135 140 Gly Ala Xaa Leu His Cys Gln Asp Ala Gly Val Pro Gly Tyr Leu Pro 145 150 155 160 Arg Glu Lys Phe Leu Arg Thr Ala Glu Ala Asp Gly Gly Leu Ala Arg 165 170 175 Thr Val Cys Gln Arg Cys Trp Leu Leu Ser His His Arg Arg Ala Leu 180 185 190 Arg Leu Gln Val Ser Arg Glu Gln Tyr Leu Glu Leu Val Ser Ala Ala 195 200 205 Leu Arg Xaa Pro Gly Pro Ser Leu Val Leu Tyr Met Val Asp Leu Leu 210 215 220 Asp Leu Pro Asp Ala Leu Leu Pro Asp Leu Pro Ala Leu Val Gly Pro 225 230 240 Lys Gln Leu Ile Val Leu Gly Asn Lys Val Asp Leu Leu Pro Gln Asp 245. 250 255 Ala Pro Gly Tyr Arg Gln Arg Leu Arg Glu Arg Leu Trp Glu Asp Cys 260 265 270 Ala Arg Ala Gly Leu Leu Leu Ala Pro Gly Thr Lys Gly His Ser Ala 275 280 285Pro Ser Arg Thr Ser His Arg Thr Gly Arg Ile Arg Ile Arg Thr 290 295 300

Gly Pro Ala Gln Trp Ser Gly Thr Cys Gly 305

<210> 346

<211> 380

<212> PRT

<213> Homo sapiens

<400> 346

Pro Ser Phe Arg Arg Glu Arg Val Glu Thr Gly Gly Gly Gly Pro Val

Thr His Gly Thr Glu Gly Pro Phe Leu Pro Leu Pro Gly Gly Thr Arg 20 25 30

Met Asn Met Thr Glm Ala Arg Val Leu Val Ala Ala Val Val Gly Leu 35 40 45

Val Ala Val Leu Leu Tyr Ala Ser Ile His Lys Ile Glu Glu Gly His 50 55 60 ...

Leu Ala Val Tyr Tyr Arg Gly Gly Ala Leu Leu Thr Ser Pro Ser Gly 65 70 75 80

Pro Gly Tyr His Ile Met Leu Pro Phe Ile Thr Thr Phe Arg Ser Val 85 90 95

Gln Thr Thr Leu Gln Thr Asp Glu Val Lys Asn Val Pro Cys Gly Thr 100 105 110

Ser Gly Gly Val Met Ile Tyr Ile Asp Arg Ile Glu Val Val Asn Met 115 120 125

Leu Ala Pro Tyr Ala Val Phe Asp Ile Val Arg Asn Tyr Thr Ala Asp 130 135 140

Tyr Asp Lys Thr Leu Ile Phe Asn Lys Ile His His Glu Leu Asn Gln 145 155 160

Phe Cys Ser Ala His Thr Leu Gln Glu Val Tyr Ile Glu Leu Phe Asp 165 170 175

Gln Ile Asp Glu Asn Leu Lys Gln Ala Leu Gln Lys Asp Leu Asn Leu 180 185 190

Met Ala Pro Gly Leu Thr Ile Gln Ala Val Arg Val Thr Lys Pro Lys 195 200 205

Ile Pro Glu Ala Ile Arg Arg Asn Phe Glu Leu Met Glu Ala Glu Lys 210 215 220

Thr Lys Leu Leu Ile Ala Ala Gln Lys Gln Lys Val Val Glu Lys Glu 225 230 235 240

Ala Glu Thr Glu Arg Lys Lys Ala Val Ile Glu Ala Glu Lys Ile Ala 245 250 255

Gln Val Ala Lys Ile Arg Phe Gln Gln Lys Val Met Glu Lys Glu Thr

260 265 Glu Lys Arg Ile Ser Glu Ile Glu Asp Ala Ala Phe Leu Ala Arg Glu 275 280 285 Lys Ala Lys Ala Asp Ala Glu Tyr Tyr Ala Ala His Lys Tyr Ala Thr 290 295 300Ser Asn Lys His Lys Leu Thr Pro Glu Tyr Leu Glu Leu Lys Lys Tyr 305 310 315 320 Gln Ala Ile Ala Ser Asn Ser Lys Ile Tyr Phe Gly Ser Asn Ile Pro 325 330 335 Asn Met Phe Val Asp Ser Ser Cys Ala Leu Lys Tyr Ser Asp Ile Arg 340 345 350Thr Gly Arg Glu Scr Ser Leu Pro Ser Lys Glu Ala Leu Glu Pro Ser 355 360 365 Gly Glu Asn Val Ile Gln Asn Lys Glu Ser Thr Gly 370 375 380 <210> 347 <211> 422 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (328) <223> Xaa equals any of the naturally occurring L-amino acids <400> 347 Trp Ser Thr Gly Asn Ala Ser Trp Glu Lys Lys Asp Asn Phe Ile Leu

1 5 10 15 Ser Ala Asp Phe Glu Met Met Gly Leu Gly Asn Gly Arg Arg Ser Met 20 25 30Lys Ser Pro Pro Leu Val Leu Ala Ala Leu Val Ala Cys Ile Ile Val 35 40 45Leu Gly Phe Asn Tyr Trp Ile Ala Ser Ser Arg Ser Val Asp Leu Gln 50 55 60 Thr Arg Ile Met Glu Leu Glu Gly Arg Val Arg Arg Arg Ala Ala Glu 65 70 75 80 Arg Gly Ala Val Glu Leu Lys Lys Asn Glu Phe Cln Gly Glu Leu Glu 85 90 95 Lys Gln Arg Glu Gln Leu Asp Lys Tle Gln Ser Ser His Asn Phe Gln 100 105 110

Leu Glu Ser Val Asn Lys Leu Tyr Gln Asp Glu Lys Ala Val Leu Val 115 120 125

Asn Asn Ile Thr Thr Gly Glu Arg Leu Ile Arg Val Leu Gln Asp Gln 130 135 140 Leu Lys Thr Leu Gln Arg Asn Tyr Gly Arg Leu Gln Gln Asp Val Leu 145 150 155 160 Gln Phe Gln Lys Asn Gln Thr Asn Leu Glu Arg Lys Phe Ser Tyr Asp 165 170 175 Leu Ser Gln Cys Ile Asn Gln Met Lys Glu Val Lys Glu Gln Cys Glu 180 190 Glu Arg Ile Glu Glu Val Thr Lys Lys Gly Asn Glu Ala Val Ala Ser 195 200 . 205 Arg Asp Leu Ser Clu Asn Asn Asp Cln Arg Gln Gln Leu Gln Ala Leu 210 215 220 Ser Glu Pro Gln Pro Arg Leu Gln Ala Ala Gly Leu Pro His Thr Glu 225 230 235 240 Val Pro Gln Gly Lys Gly Asn Val Leu Gly Asn Ser Lys Ser Gln Thr 245 250 255 Pro Ala Pro Ser Ser Glu Val Val Leu Asp Ser Lys Arg Gln Val Glu 260 265 270 Lys Glu Glu Thr Asn Glu Ile Gln Val Val Asn Glu Glu Pro Gln Arg 275 280 285 Asp Arg Leu Pro Gln Glu Pro Gly Arg Glu Gln Val Val Glu Asp Arg 290 295 300 Pro Val Gly Gly Arg Gly Phe Gly Gly Ala Gly Glu Leu Gly Gln Thr 305 310 315 320 Pro Gln Val Gln Ala Ala Leu Xaa Val Ser Glr Glu Asn Pro Glu Met 325 330 335 Glu Gly Pro Glu Arg Asp Gln Leu Val Ile Pro Asp Gly Gln Glu Glu 340 345 350 Glu Gln Glu Ala Ala Gly Glu Gly Arg Asn Gln Gln Lys Leu Arg Gly 355 360 365 Glu Asp Asp Tyr Asn Met Asp Glu Asn Glu Ala Glu Ser Glu Thr Asp 370 \$375\$Lys Gln Ala Ala Leu Ala Gly Asn Asp Arg Asn Ile Asp Val Phe Asn 385 390 395 400 Val Glu Asp Gln Lys Arg Asp Thr lle Asn Leu Leu Asp Gln Arg Glu 405 410 415

<210> 348

Lys Arg Asn His Thr Leu 420

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<211> 14
 <212> PRT
 <213> Homo sapiens
 <400> 348
Ser Leu His Arg Phe Val Leu Ser Cln Ala Lys Asp Glu Leu
<210> 349
<211> 19
<212> PRT
<213> Homo sapiens
<400> 349
Phe Ile Lys Phe Phe Ala Pro Trp Cys Gly His Cys Lys Ala Leu Ala
                                          10
Pro Thr Trp
<210> 350
<211> 19
<212> PRT
<213> Homo sapiens
<400> 350
Phe Ile Lys Phe Tyr Ala Pro Trp Cys Gly His Cys Lys Thr Leu Ala
1 5 10 15
Pro Thr Trp
<210> 351
<211> 363
<212> PRT
<213> Homo sapiens
<220>
<221> SITE
<222> (42)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 351
Arg Arg Gly Arg Gly Val Pro Gly Pro Arg Gly Arg Arg Arg Leu Trp
1 5 10 15
Ser Ala Ala Cys Gly His Cys Gln Arg Leu Gln Pro Thr Trp Asn Asp 20 25 30
Leu Gly Asp Lys Tyr Asn Ser Met Glu Xaa Ala Lys Val Tyr Val Ala 35 \hspace{1cm} 40 \hspace{1cm} 45
Lys Val Asp Cys Thr Ala His Ser Asp Val Cys Ser Ala Gln Gly Val 50 60
```

~\*

Arg Gly Tyr Pro Thr Leu Lys Leu Phe Lys Pro Gly Gln Glu Ala Val

237

65					70					75					. 80
Lys	:yr	Gln	Gly	Pro 85	Arg	Asp	Phe	Gln	Thr 90		Glu	Asn	Тгр	Met 95	
Gln	Thr	Leu	Asn 100		Glu	?ro	Val	Thr 105		Glu	Pro	Glu	Val 110	Glu	Pro
Pro	Ser	Ala 115		Glu	Leu	Lys	Gln 120		Leu	Tyr	Glu	Leu 125		Ala	Ser
Asn	Phe 130		Leu	His	Val	Ala 135	Gln	Gly	Asp	His	Phe 140	Ile	Lys	Phe	Phe
Ala 145	Pro	Trp	Cys	Gly	His 150	Cys	Ĺуs	Ala	Leu	Ala 155	Pro	Thr	Trp	Glu	Gln 160
Leu	Ala	Leu	Gly	Leu 165	Gĺu	His	Ser	Glu	Thr 170	Val	Lys	Ile	Gly	Lys 175	Val
Asp	Суѕ	Thr	Gln 180	His	Tyr	Glu	Leu	Cys 185	Ser	Gly	Asn	Gln	Val 190	Arg	Gly
Туr	Pro	Thr 195	Leu	Leu	Trp	Phe	Arg 200	Asp	Gly	Lys	Lys	Val 205	Asp	Gln	Tyr
Lys	Gly 210	Lys	Arg	Asp	Leu	Glu 215	Ser	Leu	Arg	Glu	Tyr 220	Val	Glu	Ser	Gln
Leu 225	Gln	Arg	Thr	Glu	Thr 230	Gly	Ala	Thr	Glu	Thr 235	Val	Thr	Pro	Ser	Glu 240
Ala	Pro	<b>Val</b>	Leu	Ala 245	Ala	Glu	Pro	Glu	Ala 250	Asp	Lys	Gly	Thr	Val 255	Leu
Ala	Leu	Thr	G1u 260	Asn	Asn	Phe	Asp	Asp 265	Thr	Ile	Ala	Glu	Gly 270	Ile	Thr
Phe	Ile	Lys 275	Phe	<b>ጥ</b> ሃድ	Ala	Pro	Trp 280	Cys	Gly	His	Cys	Lys 285	Thr	Leu	A <u>`</u> a
Pro	Thr 290	Trp	Glu	Glu	Leu	Ser 295	Lys	Lys	Glu	Phe	Pro 300	Gly	Leu	Ala	Gly
Val 305	Lys	Ile	Ala	Glu	Val 310	Asp	Суѕ	Thr	Ala	Glu 315	Arg	Asn	Ile	Суз	Ser 320
Lys	Tyr	Ser	Val	Arg 325	Gly	Tyr	Pro	Thr	Leu 330	Leu	Leu	Phe	Arg	Gly 335	Gly
Lys	Lys	Val	Ser 340	Glu	His	Ser	Gly	Gly 345	Arg	Ąsp	Leu	Asp	Ser 350	Leu	His
Arg	Phe	Val 355	Leu	Ser	Gln	Ala	Lys 360	Asp	Glu	Leu					

<210> 352 <211> 93

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<212> PRT
<213> Homo sapiens
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<400> 352

Het Arg Pro Gln Gly Pro Ala Ala Ser Prc Gln Arg Leu Arg Gly Leu 1 5 10 15

Leu Leu Leu Leu Leu Gin Leu Pro Ala Pro Ser Ser Ala Ser Glu 20 25 30

Ile Pro Lys Gly Lys Gln Lys Ala His Ser Gly Arg Gly Arg Trp Trp 35 40 45

Glu Thr Gly Ala Leu Gly Pro Met Ala Phe Arg Val His Leu Gly Ser 65 70 75 80

Gln Val Gly Met Asp Ser Lys Glu Lys Arg Gly Asn Val 85 90

<210> 353

<211> 273

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (210)

<223> Kaa equals any of the naturally occurring L-amino acids

<400> 353

Glu Thr Arg Val Lys Thr Ser Leu Glu Leu Leu Arg Thr Gln Leu Glu 1 5 10 15

Pro Thr Gly Thr Val Gly Asn Thr I e Met Thr Ser Gln Pro Val Pro  $\phantom{-}20\phantom{+}20\phantom{+}25\phantom{+}30\phantom{+}$ 

Asn Glu Thr Ile Ile Val Leu Pro Ser Asn Val Ile Asn Phe Ser Gln 35 40 45

Ala Glu Lys Pro Glu Pro Thr Asn Gln Gly Gln Asp Ser Leu Lys Lys 50 60

His Leu His Ala Glu Ile Lys Val Ile Gly Thr Ile Gln Ile Leu Cys 65 70 75 80

Gly Met Met Val Leu Ser Leu Gly Ile Ile Leu Ala Ser Ala Ser Phe 85 90 95

Ser Pro Asn Phe Thr Glr Val Thr Ser Thr Leu Leu Asn Ser Ala Tyr 100 105 110

Pro Phe Ile Gly Pro Phe Phe Phe Ile Ile Ser Gly Ser Leu Ser Ile 115 120 125

Ala Thr Glu Lys Arg Leu Thr Lys Leu Leu Val His Ser Ser Leu Val

239

130 135 140 Gly Ser Ile Leu Ser Ala Leu Ser Ala Leu Val Gly Phe Ile Ile Leu Ser Val Lys Gln Ala Thr Leu Asn Pro Ala Ser Leu Gln Cys Glu Leu 165 170 175 170 Asp Lys Asn Asn Ile Pro Thr Arg Ser Tyr Val Ser Tyr Phe Tyr His 180 185 190 Asp Ser Leu Tyr Thr Thr Asp Cys Tyr Thr Ala Lys Ala Ser Leu Ala 195 200 205 Gly Xaa Leu Ser Leu Met Leu Ile Cys Thr Leu Leu Glu Phe Cys Leu 210 215 220 Ala Val Leu Thr Ala Val Leu Arg Trp Lys Gln Ala Tyr Ser Asp Phe 225 Pro Gly Ser Val Leu Phe Leu Pro His Ser Tyr Ile Gly Asn Ser Gly 245 250 255 Met Ser Ser Lys Met Thr His Asp Cys Gly Tyr Glu Glu Leu Leu Thr 260 265 270 Ser <210> 354 <211> 192 <212> PRT <213> Homo sapiens <220> <221> SITE <222> (129) <223> Xaa equals any of the naturally occurring L-amino acids <400> 354 Met Het Val Leu Ser Leu Gly Ile Ile Leu Ala Ser Ala Ser Phe Ser 1 5 10 15 Pro Asn Phe Thr Gln Val Thr Ser Thr Leu Leu Asn Ser Ala Tyr Pro  $20 \ 25 \ 30$ Phe Ile Gly Pro Phe Phe Phe Ile Ile Ser Gly Ser Leu Ser Ile Ala 35Thr Glu Lys Arg Lou Thr Lys Leu Leu Val His Ser Ser Leu Val Gly 50 60 Ser Ile Leu Ser Ala Leu Ser Ala Leu Val Gly Phe Ile Ile Leu Ser 65 70 75 80 Val Lys Gln Ala Thr Leu Asn Pro Ala Ser Leu Gln Cys Glu Leu Asp 85 90 95

PCT/US99/17130 WO 00/06698

Lys Asn Asn Ile Pro Thr Arg Ser Tyr Val Ser Tyr Phe Tyr His Asp

Ser Leu Tyr Thr Asp Cys Tyr Thr Ala Lys Ala Ser Leu Ala Gly
115 120 125

Xaa Leu Ser Leu Met Leu Ile Cys Thr Leu Leu Glu Phe Cys Leu Ala 130 140

Val Leu Thr Ala Val Leu Arg Trp Lys Gln Ala Tyr Ser Asp Phe Pro 145 150 155 160

Gly Ser Val Leu Phe Leu Pro His Ser Tyr Ile Gly Asn Ser Gly Met 165 170 175

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<210> 355 <211> 204

<212> PRT <213> Homo sapiens

<220>

<221> SITE <222> (119)

<223> Xaa equals any of the naturally occurring L-amino acids

Gly Ala Ser Cys Glu Gly Gly Gly Ala Ala Arg Ala Ala Leu Gly
1 10 15

Val His Arg Ser Gln Lys Ala Leu Leu Val Phe Arg Arg Thr Leu Ser 20 25 30

As n Leu Tyr Met Pro Leu Leu Arg Gly Leu Leu Trp Leu Gln Val 35 40 45

Leu Cys Ala Gly Pro Leu His Thr Glu Ala Val Val Leu Leu Val Pro 50 55 60

Ser Asp Asp Gly Arg Ala Phe Leu Leu Arg Ser Arg Leu Leu His Pro 65 70 75 80

Glu Ala His Val Pro Pro Ala Ala Asp Arg Gly Ala Ser Leu Gln Cys 85 90 95

Val Leu His Gln Ala Ala Pro Lys Ser Arg Pro Arg Ser Pro Ala Ala 100 105 110

Gly Ala Ala Leu Leu His Xaa Pro Arg Arg Thr Gly Asp Glu Pro Cys

Arg Glu Phe His Gly Asn Gly Phe Pro Gly Pro Thr Gln Leu Thr Pro 130 135 140

Cly Glu Cys Gly Leu Pro Ale Pro Ser Ser Leu Leu Gln His Ala Ser 145 150 155 160

241

Ala Pro Val Arg Thr Gly Ser Glu Gly Gln Val Val Gly Cys Pro Arg 165 170 175

Ala arg Gly Glu Thr Gly Glu Gly Leu Ser Leu Ala Phe Leu Ser Ser 180  $$185\$ 

Leu Met Phe Thr Ser Arg Asn Gly Leu Val Gly Cys

<210> 356 <211> 72

<212> PRT

<213> Homo sapiens

Met Gly Ser Ala Ala Leu Glu Ile Leu Gly Leu Val Leu Cys Leu Val 1 5 10 15

Gly Trp Gly Gly Leu Ile Leu Ala Cys Gly Leu Pro Met Trp Gln Val  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Thr Ala Phe Leu Asp His Asn Ile Val Thr Ala Gin Thr Thr Trp Lys 35 40 45

Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly Thr Cys Ser Ala  $50 \\ \hspace{1.5cm} 55 \\ \hspace{1.5cm} 60$ 

Lys Cys Thr Thr Arg Cys Trp Leu 65 70

<210> 357

<211> 115

<212> PRT <213> Homo sapiens

Leu Lys Arg Ala Pro Pro Gly Pro Ala Leu Ala Lys Gly Leu Leu Gln
1 5 10 15

Arg Arg His Ser Thr Ala Val Val Ile Arg Glu Met Thr Ser Tyr Ile 35  $\phantom{\bigg|}40\phantom{\bigg|}45\phantom{\bigg|}$ 

Leu Ile Ser Phe Val Leu Leu Ile Gly Val Gly Cys Ile Glu Lys Asp  $50 \hspace{1cm} 55 \hspace{1cm} 60$ 

Gln Ser Cys Pro Val Phe Gly Gly Arg Lys Arg Leu His Leu Leu Phe 65 70 75 80

Val Gly Gly Gln Leu Arg Gln Val Arg Met Leu Arg Gly Glu Leu Ser 85 90 95

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                                  105
Thr Cys Phe
        115
<210> 358
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<212> PRT
<213> Homo sapiens
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Val Ile Lys Leu Ile Cys Pro Ala Ala Phe Pro Val Tyr Phe Gln Asp
1 5 10 15
Met Ala Arg Gly Cys Val Cys Ser Leu Cys Ala Ser Val Cys Ile Phe 20 25 30
Leu Ser Ser Leu Phe Pro Leu Leu Pro Ser Val His Ser Val Asn Ile
                              40
Ile Ser Cys Leu Leu Leu Ser Lys Cys Phe Glu Gly Leu Glu Leu Met 50 60
Cys Glu His Leu Tyr Gln Leu Ser Gln Leu His Val Leu His His Ile
65 70 75 80
Phe Ser Tyr Leu Leu Cys Thr Pro
<210> 359
<211> 716
<212> PRT
<213> Homo sapiens
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<220>
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<220>
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<222> (705)
<223> Xaa equals any of the naturally occurring L-amino acids
<400> 359
Tyr Xaa Ile Pro Gly Ser Thr His Ala Ser Gly Arg Glr Arg Gly Ser
Gly Arg Gly Glu Asp Asp Ser Gly Pro Pro Pro Ser Thr Val Ile Asn
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		35					40			. Lys	· FIU	45		. vai	. Gir
Gln	Ala 50	Arg	Ile	Ala	Gln	Asn 55	Gly	Ile	Leu	Gly	Asp 60		Ile	Ile	Arg
<u>∓</u> γ <u>∓</u> 65	Asp	۷a۱	Asn	Arg	Glu 70	Gln	Ser	Ile	Gly	Asp 75		Gln	Val	Leu	Asn 80
Gly	Tyr	Phe	Val	His 85	Tyr	Phe	Ala	Pro	Lys 90		Leu	Pro	Pro	Leu 95	
Lys	Asn	Val	Val 100	Phe	Val	Leu	Asp	Ser 105		Ala	Ser	Met	Val 110		Thr
Lys	Leu	Arg 115	Gln	Thr	Lys	А́Бр	Ala 120	Leu	Phe	Thr	Ile	Leu 125	His	qeA	Leu
Arg	Pro 130	Gln	Asp	Arg	Phe	Ser 135	Ile	Ile	Gly	Phe	Ser 140	Asn	Arg	Ile	Lys
Val 145	Trp	Lys	Asp	His	Leu 150	Ile	Ser	Val	Thr	Pro 155	Asp	Ser	Ile	Arg	Asp 160
Gly	Lys	Val	Tyr	Ile 165	His	His	Met	Ser	Pro 170	Thr	Gly	Gly	Thr	Asp 175	Ile
Asn	Gly	Val	Leu 180	Gln	Arg	Ala	Ile	Arg 185	Leu	Leu	Asn	Lys	Tyr 190	Va1	Ala
His	Ser	Gly 195	Ile	Gly	qeA	Arg	Ser 200	Val	Ser	Leu	Ile	Val 205	Phe	Leu	Thr
Asp	Gly 210	Lys	Pro	Thr	Val	Gly 215.		Thr	His	Thr	Leu 220	Lys	Ile	Leu	Asn
Asn 225	Thr	Arg	Glu	Ala	Ala 230	Arg	Gly	Gln	Val	Сув 235	Ile	Phe	Thr	Ile	Gly 240
Ile	Gly	Asn	Asp	Val 245	Asp	Phe	Arg	Seu	Leu 250	Glu	Lys	Leu	Ser	Leu 255	Glu
Asn	Суѕ	Gly	Leu 260	Thr	Arg	Arg	Val	His 265	Glu	Glu	Glu	Asp	Ala 270	Gly	Ser
Gln	Leu	Ile 275	Gly	Phe	Tyr	Asp	Glu 280	Ile	Arg	Thr	Pro	Leu 285	Leu	Ser	Asp
Ile	Arg 290	Ile	Asp	Tyr	Pro	Pro 295	Ser	Ser	Val	Val	Gln 300	Ala	Thr	Lys	Thr
Leu	Phe	Pro	Asn	Tyr	Phe	Asn	Gly	Ser	Glu	Ile	Ile	Ile	Ala	Gly	Lys

Leu Val Asp Arg Lys Leu Asp His Leu His Val Glu Val Thr Ala Ser 325 and Ser Lys Lys Phe Ile Ile Leu Lys Thr Asp Val Pro Val Arg Pro

			340	)				345	5				350	)	
Gln	Lys	355	Gly	Lys	ask i	Val	Thr 360	Gly	/ Ser	Pro	Arg	Pro 365		Gly	' Asp
Gly	Glu 370	Gly	Asp	Хаа	<b>A</b> sn	His 375	Ile	: Clu	Arg	Leu	Trp 380		Туг	Leu	Thr
Thr 385	Lys	Glu	Leu	Leu	Ser 390	Ser	Trp	Leu	Gln	Ser 395	Asp	Asp	Glu	Pro	Glu 400
Lys	Glu	Arg	Leu	Arg 405	<b>Gl</b> n	Arg	Ala	Gln	Ala 410	Leu	Ala	Val	Ser	Туг 415	Arg
Phe	Leu	Thr	Pro 420	Phe	Thr	Ser	Met	Lys 425	Leu	Arg	Gly	Pro	Val 430	Pro	Arg
Met	Asp	Gly 435	Leu	Glu	Glu	Ala	His 440	Gly	Met	Ser	Ala	Ala 445		Gly	Pro
Glu	Pro 450	Val	Val	Gln	Ser	Val 455	Arg	Gly	Ala	Glγ	Thr 460	Gln	Pro	Gly	Pro
Leu 465	Leu	Lys	Lys	Pro	Туг 470	Gln	Pro	Arg	Ile	Lys 475	Ile	Ser	Lys	Thr	Ser 480
Val	Asp	Gly	Asp	Pro 485	His	Phe	Val	Val	Asp 490	Phe	Pro	Leu	Ser	Arg 495	Leu
Thr	Val	Cys	Phe 500	Asn	Ile	Asp	Gly	Gln 505	Pro	Gly	Asp	Ile	Leu 510	Arg	Leu
<b>V</b> al	Ser	Asp 515	His	Arg	Asp	Ser	Gly 520	Val	Thr	Va1	Asn	Gly 525	Glu	Leu	Ile
GĮĀ	Ala 530	Pro	Ala	Pro	Pro	Asn 535	Gly	His	Lys	Lys	Gln 540	Arg	Thr	Туг	Leu
Arg 545	Thr	Ile	Thr	Ile	Leu 550	Ile	Asn	Lys	Pro	Clu 555	Arg	Ser	Tyr	Leu	Glu 560
Ile	Thr	Pro	Ser	Arg 565	Val	Ile	Leu	Asp	Gly 570	Gly	Asp	Arg	Leu	Val 575	Leu
Pro	Cys	Asn	Gln 580	Ser	Val	Val	Val	Gly 585	Ser	Trp	Gly	Leu	Glu 590	Val	Ser
Val	Ser	A1a 595	Asn	Ala	Asn	Val	Thr 600	Val	Thr	Ile	Gln	Gly 605	Ser	Ile	Ala
Phe	Val 610	Ile	Leu	Ile	His	Leu 615	Туг	Lys	Lys	Pro	Ala 620	Pro	Phe.	Gln	Arg
His 625	His	Leu	Gly	Phe	Туr 630	Ile	Ala	Asn	Ser	Glu 635	Gly	Leu	Ser	Ser	Asn 640
Cys	His	Gly	Leu	Leu 645	Gly	Gln	Phe	Leu	Asn 650	Gln	Asp	Ala	Arg	Leu 65 <b>5</b>	Thr

Glu Asp Pro Ala Gly Pro Ser Gln Asn Leu Thr His Pro Leu Leu Leu 660 . 665 . 665 . 670 .

Gln Val Gly Glu Gly Pro Glu Ala Val Leu Thr Val Lys Gly His Gln 675 680 685

Val Pro Val Val Trp Lys Gln Arg Lys Ile Tyr Asn Gly Glu Glu Gln 690 695 700

Xaa Asp Cys Trp Phe Ala Arg Asn Met Pro Pro Asn 705 710 715

<210> 360

<211> 387

<212> PRT

<213> Homo sapiens

<400> 360

Pro Arg Val Arg Ser Ile Lys Val Thr Glu Leu Lys Gly Leu Ala Asn
1 5 10 15

His Val Val Gly Ser Val Ser Cys Glu Thr Lys Asp Leu Phe Ala 20 25 30

Ala Leu Pro Gln Val Val Ala Val Asp Ile Asn Asp Leu Gly Thr Ile  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Lys Leu Ser Leu Glu Val Thr Trp Ser Pro Phe Asp Lys Asp Asp Gln 50 55 60

Pro Ser Ala Ala Ser Ser Val Asn Lys Ala Ser Thr Val Thr Lys Arg 65 70 75 80

Phe Ser Thr Tyr Ser Gln Ser Pro Pro Asp Thr Pro Ser Leu Arg Glu 85 90 95

Gln Ala Phe Tyr Asn Met Leu Arg Arg Gln Glu Glu Leu Glu Asn Gly 100 . 105 110

Thr Ala Trp Ser Leu Ser Ser Glu Ser Ser Asp Asp Ser Ser Ser Pro 115 120 125

Gln Leu Ser Gly Thr Ala Arg His Ser Pro Ala Pro Arg Pro Leu Val

Gln Gln Pro Glu Pro Leu Pro Ile Gln Val Ala Phe Arg Arg Pro Glu 145 150 155 160

Thr Pro Ser Ser Gly Pro Leu Asp Glu Glu Gly Ala Val Ala Pro Val 165 170 175

Leu Ala Asn Gly His Ala Pro Tyr Ser Arg Thr Leu Ser His Ile Ser 180 185 190

Glu Ala Ser Val Asn Ala Ala Leu Ala Glu Ala Scr Val Glu Ala Val 195 200 205

Gly Pro Lys Ser Leu Ser Trp Gly Pro Ser Pro Pro Thr His Pro Ala

210 215 220 Pro Thr His Gly Lys His Pro Ser Pro Val Pro Pro Ala Leu Asp Pro 225 230 235 240 Gly His Ser Ala Thr Ser Ser Thr Leu Gly Thr Thr Gly Ser Val Pro 245 250 255 Thr Ser Thr Asp Pro Ala Pro Ser Ala His Leu Asp Ser Val His Lys 260 265 270 Ser Thr Asp Ser Gly Pro Ser Glu Leu Pro Gly Pro Thr His Thr Thr 275 280 285 Thr Gly Ser Thr Tyr Ser Ala Ile Thr Thr Thr His Ser Ala Pro Ser 290 295 300 Pro Leu Thr His Thr Thr Gly Ser Thr His Lys Pro Ile Ile Ser 305 310 315 320 Thr Leu Thr Thr Gly Pro Thr Leu Asa Ile Ile Gly Pro Val Gln  $325 \ \ 330 \ \ 335$ Thr Thr Thr Ser Pro Thr His Thr Met Pro Ser Pro Ser Ser His Ser 340 345 350Asn Ser Pro Gln Tyr Val Asp Phe Cys Ser Ser Val Cys Asp Asn Ile 355 360 365 Phe Val His Tyr Val Ile Gly Ile Phe Phe His Thr Leu Tyr Ser Ser 370 375 380 Lys Thr Leu 385 <210> 361 <211> 260 <212> PRT <213> Homo sapiens Pro Arg Val Arg Ser Ile Lys Val Thr Glu Leu Lys Gly Leu Ala Asn 1 5 10 15 His Val Val Gly Ser Val Ser Cys Glu Thr Lys Asp Leu Phe Ala 20 25 30 Ala Leu Pro Gln Val Val Ala Val Asp Ile Asn Asp Leu Gly Thr Ile  $35 \ 40 \ 45$ Lys Leu Ser Leu Glu Val Thr Trp Ser Pro Phe Asp Lys Asp Asp Gln 50 55 60 Pro Ser Ala Ala Ser Ser Val Asn Lys Ala Ser Thr Val Thr Lys Arg 65 70 75 80 Phe Ser Thr Tyr Ser Glr Ser Pro Pro Asp Thr Pro Ser Leu Arg Glu 85 90 95

Gln Ala Phe Tyr Asn Mot Leu Arg Arg Gln Glu Glu Leu Glu Asn Gly 100 105 110Thr Ala Trp Ser Leu Ser Ser Glu Ser Ser Asp Asp Ser Ser Ser Pro 115 120 125 Gln Leu Ser Gly Thr Ala Arg His Ser Pro Ala Pro Arg Pro Leu Val Gln Gln Pro Glu Pro Leu Pro Ile Gln Val Ala Phe Arg Arg Pro Glu 145 150 155 160 Thr Pro Ser Ser Gly Pro Leu Asp Glu Glu Gly Ala Val Ala Pro Val
165 170 175 Leu Ala Asn Gly His Ala Pro Tyr Ser Arg Thr Leu Ser His Ile Ser 180  $$185\$ Glu Ala Ser Val Asn Ala Ala Leu Ala Giu Ala Ser Val Glu Ala Val 195 200 205 Gly Pro Lys Ser Leu Ser Trp Gly Pro Ser Pro Pro Thr His Pro Ala 210 215 220 Pro Thr His Gly Lys His Pro Ser Pro Val Pro Pro Ala Leu Asp Pro 225 230 235 Gly His Ser Ala Thr Ser Ser Thr Leu Gly Thr Thr Gly Ser Val Pro  $245 \hspace{1cm} 250 \hspace{1cm} 255 \hspace{1cm}$ Thr Ser Thr Asp 260 <210> 362

<211> 155

<212> PRT

<213> Homo sapiens

<400> 362

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Met Glu Ala Val Val Phe Val Phe Ser Leu Leu Asp Cys Cys Ala Leu 20 25 30

Ile Phe Leu Ser Val Tyr Phe Ile Ile Thr Leu Ser Asp Leu Glu Cys  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Asp Tyr Ile Asn Ala Arg Ser Cys Cys Ser Lys Leu Asn Lys Trp Val 50 . 55 60

Ile Pro Glu Leu Ile Gly His Thr Ile Val Thr Val Leu Leu Leu Met 65 70 75 80

Ser Leu His Trp Phe Ile Phe Leu Leu Asn Leu Pro Val Ala Thr Trp 85 90 95

PCT/US99/17130 248

As n Ile Tyr Arg Tyr Ile Met Val Pro Ser Gly As n Met Gly Val Phe 100 \$100\$

Asp Pro Thr Glu Ile His Asn Arg Gly Gln Leu Lys Ser His Met Lys 115 120 125

Glu Ala Met Ile Lys Leu Gly Phe His Leu Leu Cys Phe Phe Met Tyr 130 135 140

Leu Tyr Ser Met Ile Leu Ala Leu Ile Asn Asp 145 150 155

<210> 363 <211> 70 <212> PRT

<213> Homo sapiens

Ala Arg Ala Pro Ala Pro Ser Leu Pro Pro Leu Pro Ser Pro Ala Pro 1 5 10 15

Ala Leu Ala Pro Ala His Ser Leu Leu Gly Leu Leu Leu Gly Arg Met 20 25 30

Ser Gly Ser Ser Leu Pro Ser Ala Leu Ala Leu Ser Leu Leu Val  $35\,$ 

Ser Gly Ser Leu Leu Pro Gly Pro Gly Ala Ala Gln Asn Val Arg Val 50 \$55\$

Gln Ser Gly Gln Asp Gln 65 70

<210> 364 <211> 56 <212> PRT

<213> Homo sapiens

<400> 364

Gly Thr Ser Lys Asp Cys Val Leu Tyr Ala Phe Leu Asp Pro Gly Met 1 5 10 15

Ala Val Pro Leu Phe Leu Tyr Ile Phe Thr Leu Leu Pro Leu Leu Pro 20 25 30

Phe Leu Leu Ser Leu Cys Phe Ser Pro Leu Thr Val Lys Arg Ser Ser 35 40 45

Ser Ser Glu Ser Lys Ser Ser Leu

Applicant's or agent's file reference number	PZ031PCT	International application	Unassigned

# INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

A. The indications made below relate to the microorganism referred to in the description on page 280 line NVA WIPO PC  B. IDENTIFICATIONOF DEPOSIT Further deposits are identified on an additional sheet. Name of depositary institution. American Type Culture Collection  Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209  United States of America  Date of deposit July 27, 1998 C03069  C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet.	
on page 260 line NA WIPO PC  B. IDENTIFICATIONOF DEPOSIT Further deposits are identified on an additional sheet  Name of depositary institution American Type Culture Collection  Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209  United States of America  Date of deposit  July 27, 1998  Accession Number  203069	39
B. IDENTIFICATIONOF DEPOSIT  Further deposits are identified on an additional sheet  Name of depositary institution Arrierican Type Culture Collection  Address of depositary institution (including postal code and country)  10801 University Boulevard  Manassas, Virginia 20110-2209  United States of America  Date of deposit  July 27, 1998  Accession Number  203069	7
Name of depositary institution American Type Culture Collection  Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America  Date of deposit  July 27, 1998  203069	
Address of depositary institution (including postal code and country)  10801 University Boulevard Manassas, Virginia 20110-2209 United States of America  Date of deposit  July 27, 1998  Accession Number 203069	
10801 University Boulevard Manassas, Virginia 20110-2209 United States of America  Date of deposit  July 27, 1998  Accession Number 203069	
Manassas, Virginia 20110-2209 United States of America  Date of deposit  July 27, 1998  Accession Number 203069	
United States of America  Date of deposit  July 27, 1998  Accession Number  203069	
July 27, 1998 203069	
July 27, 1998 203069	
C Apperent	$\dashv$
C. ADDITIONAL INDICATIONS (leave blank if not applicable)  This information is continued on an additional sheet	_
	$\exists$
	ı
•	
·	ı
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	-
Europe	-
In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28(4) EPC).	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	=
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., 'Accessing Number of Deposit')	D22
Formering Officers	
For International Bureau use only  This sheet was received with the international application  This sheet was received by the International Application	7
This sheet was received with the international application  This sheet was received by the International Bureau on:  1 8 AUGUST 1999	
Authorized officer A Authorized officer	
PCT General Division	4

Form PCT/RO/134 (July 1992)

#### CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

#### NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

### **AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

### **FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

# UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

### DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

## NETHERLANDS.

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

Applicant's or agent's file	PZ031PCT	International application	<del>"</del>
reference number	P2031PC1		Unassigned

# INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

on page 243 , line	N/A .
B. IDENTIFICATIONOF DEPOSIT	Further deposits are identified on an additional sheet
Name of depositary institution American Type Culture C	Collection
er F	
Address of depositary institution tinclading postal code and o	country)
10801 University Boulevard	• •
Manassas, Virginia 20110-2209 United States of America	
Officed States of America	
Date of deposit	Accession Number
June 11, 1998	209965
C. ADDITIONAL INDICATIONS (leave blank if not appli	icable) This information is continued on an additional sheet
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D. DESIGNATED STATES FOR WHICH INDICAT	TONS ARE MADE ISLANDARY
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Form PCT/RO/134 (July 1992)

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

### **NORWAY**

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

# **AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

## **FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

### UNITED KINGDOM

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

### **SWEDEN**

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### **NETHERLANDS**

Applicant's or agent's file reference number	PZ031PCT	International application	Unassigned
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# INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indication	s made below relate to the r		
оправе	249	, line	N/A
R IDENTIFICA	TIONOFDEPOSIT		
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Name of depositur	institution American Ty	pe Culture Colle	ection
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Address of denos	itary institution (including	mercal ands and same	
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10801 Universit	ly Boulevard inia 20110-2209		
United States of	f America		
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	June 26, 1998		203027
C. ADDITIONA	AL INDICATIONS (leave	e blank if not applicab	le) This information is continued on an additional sheet
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Form PCT/RO/134 (July 1992)

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

#### NORWAY

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## **AUSTRALIA**

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## **FINLAND**

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### UNITED KINGDOM

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#### **SWEDEN**

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# **NETHERLANDS**

Applicant's or agent's file	<del></del>	International application	
reference number	PZ031PCT	tructuational application	Unassigned

# INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

A. The indications made below relate to the microorganism refer on page 253, line	red to in the description N/A				
B. IDENTIFICATIONOF DEPOSIT	Further deposits are identified on an additional sheet				
Name of depositary institution American Type Culture Collection					
Address of depositary institution (including postal code and count 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	(m)				
Date of deposit	Accession Number .				
July 27, 1998	203071				
C. ADDITIONAL INDICATIONS(leave blank if not applicable	This information is continued on an additional sheet				
D. DESIGNATED STATES FOR WHICH INDICATION Europe In respect to those designations in which a European Produced in the publication or until the date on which application has been refused the issue of such a sample to an expert nominated by the same of such a sample to an expert nominated by the same of such a sample to an expert nominated by the same of such a sample to an expert nominated by the same of such a sample to an expert nominated by the same of such a sample to an expert nominated by the same of such a sample to an expert nominated by the same of such as a sample to an expert nominated by the same of such as a sample to an expert nominated by the same of such as a sample to an expert nominated by the same of such as a sample to an expert nominated by the same of same of such as a sample to an expert nominated by the same of	atent is sought a sample of the deposited on of the mention of the grant of the European patent or withdrawn or is deemed to be withdrawn, only by se person requesting the sample (Rule 28(4) EPC).				
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Form PCT/RO/134 (July 1992)

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

#### **NORWAY**

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## UNITED KINGDOM

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# **NETHERLANDS**

Applicant's or agent's file eference number	PZ031PCT	International application	 _,

# INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13öis)

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Form PCT/RO/134 (July 1992)

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

### NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

## **AUSTRALIA**

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

# **FINLAND**

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

#### UNITED KINGDOM

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

#### **SWEDEN**

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

# **NETHERLANDS**

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/17130

<u></u>						
A. CLASSIFICATION OF SUBJECT MATTER						
IPC(6) :Please See Extra Sheet.						
US CI. :Picase See Extra Sheet.  According to International Patent Classification (IPC) or to both national classification and IPC						
B. FIELDS SEARCHED						
	41.4.7.2.11					
Minimum documentation searched (classification system follow						
U.S. : 536/23.1, 23.5; 435/69.1, 320.1, 252.3, 325, 6, 7.1;						
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched						
Electronic data base consulted during the international search (i APS, DIALOG - Biotech Files	name of data base and, where practicable, search terms used)					
C. DOCUMENTS CONSIDERED TO BE RELEVANT						
Category* Citation of document, with indication, where a	ppropriate, of the relevant passages Relevant to claim No.					
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A JACOBS, K. A. et al. A Genetic S						
Encoding Secreted Proteins. Gene.	1997, Vol. 198, pages 289-					
296, see entire document.						
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Further documents are listed in the continuation of Box (	See patent family annex.					
Special emigeries of cited documents:	'T' later document published after the international filing data or priority					
A* document defining the general state of the est which is not considered to be of particular relevance	date and not in conflict with the application but aired to understand the principle or theory underlying the invention					
"B" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be					
"L" document which may throw doubts on priority (laim(s) or which is cited to establish the publication date of establish or other	considered novel or cannot be considered to involve an inventive step when the document is taken slone					
cited to establish the publication date of enother citation or other special reason (as specified)	"V" document of annimum animum a 1 to 1 to 1					
"O" document referring to an oral disclosure, use, exhibition or other	combined with one or more other such documents, such combination					
P document published prior to the interestional filing data but later than	occurs con some to a beamen actives to the ext					
the priority date claimed  Date of the actual completion of the international search	Date of mailing of the international search report					
······································	21 OCT 1999					
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks	Authorized officer					
Box PCT Washington, D.C. 20231	FLEXABETH C. KEMMERER LOL.					
Facsimile No. (703) 305-3230	Telephone No. (703) 308-G196					
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Form PCT1SA 210 (second sheet)(July 1992)\*

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/17130

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)				
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
Claims Nos.:  because they relate to subject matter not required to be searched by this Authority, namely:				
Claims Nos.: 1-23     because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  Please See Extra Shoet.				
Claims Nos.:     because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).				
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)				
This International Searching Authority found multiple inventions in this international application, as follows:				
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.				
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.				
3. As only some of the required additional search fees were timely paid by the applicant, this international search report cover only those claims for which fees were paid, specifically claims Nos.:				
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:				
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.				

Form PCT/ISA/210 (continuation of first sheet(1))(July 1992) a

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/17130

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

C12N 1/21, 5/10, 15/11, 15/12, 15/63; A61K 38/16, 38/17; C07K 14/00, 14/435, 16/00; G01N 33/50

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

536/23.1, 23.5; 435/69.1, 320.1, 252.3, 325, 6, 7.1; 530/350, 300, 387.1; 514/2

BOX I. OBSERVATIONS WHERE CLAIMS WERE FOUND UNSEARCHABLE 2. Where no meaningful search could be carried out, specifically:

All of the claims were unsearchable to the extent that they require reference to sequences from the sequence listing or an ATCC deposit. However, the specific sequence and deposit numbers were replaced in the claims with generic designators X, Y and Z. Therefore, no meaningful search of the sequences or deposits per se can be carried out by this Authority. The subject matter of the claims has been searched only to the extent possible with reference to the balance

of the description.

Form PCT/ISA/210 (extra sheet)(July 1992)\*